TRANSACTIONS & STUDIES

of the

College of Physicians

of

Philadelphia

FOURTH SERIES

VOLUME 21

1953-54

WAVERLY PRESS, INC.
Baltimore, Md.

The College of Physicians of Philadelphia does not assume responsibility for statements or views expressed by contributors to the *Transactions & Studies.* The editor checks bibliographic references, to aid in making them factually reliable, and occasionally supplies headings in the text, to facilitate reference to clearly defined portions of the text; the communications are in other respects printed exactly as they were submitted, subject to author corrections on the galleys.

An index to the annual volume of the *Transactions & Studies* appears in the fourth and final (April) number of the volume.

The scientific and historical communications are indexed in: *Biological Abstracts; Current List of Medical Literature; Quarterly Cumulative Index Medicus.*

The Transactions & Studies of the College of Physicians of Philadelphia is published four times a year—June, August, February, April—at Baltimore, Maryland by the College of Physicians of Philadelphia. Subscription, $2 a volume. Single copies, 75 cents.

Publication Office: Mt. Royal and Guilford Aves., Baltimore 2, Md. *Editorial correspondence* should be addressed to: The Editor, College of Physicians of Philadelphia, 19 South 22d Street, Philadelphia-3, Pa. Entered as second class matter June 21, 1938, at the Post Office at Baltimore, Md., under the act of August 24, 1912.

Printed in U. S. A.

Contents

NO. 1, JUNE, 1953

A Report on Microscopic Progress in the Chemotherapy of Cancer
(*Nathan Lewis Hatfield Lecture XXXVII*) ..... *Stanley P. Reimann* 1
Medical Students and Their Examiners in Eighteenth Century America .... *Whitfield J. Bell, Jr.* 14
Memoirs
James Harold Austin (1883–1952) ..... *O. H. Perry Pepper* 25
George Woodward (1863–1952) ..... *William U. McClenahan* 28
List of Contributors to the Building, Development, and Austin Funds, and to the Library of the College 31

NO. 2, AUGUST, 1953

The Evaluation of the Adaptation Concept in Relation to the Connective Tissue Diseases
(*Benjamin Musser Lecture IV*) ..... *Walter Bauer* 39
Epidemiologic and Clinical Studies on Brucellosis, 1937–1952
(*James M. Anders Lecture XXIX*) ..... *Wesley W. Spink* 51
The Vanishing Spas of Pennsylvania. An Historical Review. Part I.
Igho H. Kornblueh and Geo. Morris Piersol 63
Memoir
Alexander Randall (1883–1951) ..... *Charles A. W. Uhle* 78
Transactions of the Sections: Programs, and Abstracts from the Section on General Medicine 80
Pathological Society of Philadelphia
Proceedings of the Meetings, including Abstracts, October, 1952–May, 1953 90

NO. 3, FEBRUARY, 1954

The Present Status of Intracardiac Surgery for Mitral and Aortic Stenosis
(*Thomas Dent Mütter Lecture LXVI*) ..... *Robert P. Glover* 97
Isotope Dilution: a Theory, a Method, a Pathway to New Horizons
(*Alvarenga Prize Lecture XIII*) ..... *Francis D. Moore* 106
The Vanishing Spas of Pennsylvania. An Historical Review. Part II.
Igho H. Kornblueh and Geo. Morris Piersol 119
Memoir
Edwin Grant Conklin (1863–1952) ..... *E. B. Krumbhaar* 131

NO. 4, APRIL, 1954

President's Address ..... *Richard A. Kern* 133
Annual Reports
Library 138
Mütter Museum and College Collections 151
Sections 153
Memoirs
Edwin E. Graham (1864–1953) ..... *Edward L. Bauer* 156
Warfield Theobald Longcope (1877–1953) ..... *Francis D. W. Lukens* 158
B. B. Vincent Lyon (1880–1953) ..... *Martin E. Rehfuss* 160
Transactions of the Sections: Programs, and Abstracts from the Section on General Medicine 162
List of College Lectures, 1953 168
Officers, Committees, Sections, and Administrative Staff of the College, 1954 169
List of the Fellows 172
Index to Volume 21 193

Digitized by the Internet Archive
in 2013

http://archive.org/details/transactionsstud4211coll

TRANSACTIONS & STUDIES

of the

College of Physicians of Philadelphia

Volume 21 (Fourth Series)

Number 1 (June 1953)

A Report on Microscopic Progress in the Chemotherapy of Cancer*

By STANLEY P. REIMANN, M.D.

Director, Lankenau Hospital Research Institute, and Scientific Director, Institute for Cancer Research, Philadelphia

FIRST, I express appreciation for the honor of presenting this Nathan Lewis Hatfield Lecture. My first idea was to make lists of proposed remedies for cancer, beginning with the oldest known, but I soon found, as an understatement, that it was hardly practicable.

I have here a stack of cards of references and abstracts for a little less than a year, and here is a volume prepared by Helen M. Dyer of the National Cancer Institute in 1949, just listing substances which have been scrutinized for their anti-cancer effects.

In the March 1952 issue of *Cancer Research* there began publication of condensed information on compounds shown to be inactive on neoplastic growths. This is to continue.

Further, Wolff devotes one big volume of his five on cancer to methods of treatment which include chemotherapeutic efforts.

Therefore, rather than to review and list many of the attempts at chemotherapy carried on in the last few years, I prefer to approach the subject from more basic angles, such as the philosophy underlying the use of many of the substances tried. It makes it more interesting to me, and I hope it will to you, to consider the ideas, for example, as to the "cause" of cancer which prompted the arguments that such and such a procedure or substance should be used. Not the least of the fascinations of the subject is comparison of our present research with that of the past.

We can safely say that not one of the physicians of olden times whose name has persisted and been honored in medical history has failed to include cancer and its treatment in thought and writing. Even though they began with mighty scanty knowledge and often with false premises, their logic from those premises and the facts at hand is unassailable. And they knew how to ask questions—many of which we're bound to say are not only pertinent but remain unanswered today.

From ancient times there were two schools of thought as to the cause of cancer—the local and the constitutional. Is cancer purely a local disease or does it have a constitutional background, or are some cancers local and others the result of a "diathesis"—that useful word meaning so much and yet so little?

* Nathan Lewis Hatfield Lecture XXXVII, College of Physicians of Philadelphia, 4 February 1953.

How do we answer these questions today? Both ways, I believe. Kangri cancers, x-ray cancers of the fingers and hands, aniline cancers of the bladder, pipe-smokers' cancer of the lip, we believe are local in origin, but we leave an escape hatch for ourselves when we say that not every traditional Irishman whose short, hot clay pipe stem rests on one corner of his lip, develops cancer at this spot.

Lymphosarcoma we readily believe has constitutional help in its development. The same thought applies to others, even those of local beginnings such as carcinoma of the breast. We know, too, that even the most potent carcinogens synthesized, such as benzpyrene or methylcholanthrene, do not produce cancer in 100% of random mice. We can inbreed and backcross to increase susceptibility. Dimethylaminoazobenzene produces cancer of the liver in rats, but its carcinogenicity can be reduced by riboflavin, B_{12} and other dietary manipulations, or, conversely, its effects in time and numbers can be enhanced by biotin and other additions and/or subtractions.

The flow of thought for therapy directed by these facts leads to the conclusion that not all cancers are alike and no one treatment, outside of complete removal or destruction, is among the probabilities. We, as many others, have been more and more practicing the use of several procedures in a given case, even though judgment of effectiveness of any one is obscured by adding variables. In human beings the strictly scientific must give way to the humanitarian. But the variability of cancers was known to the older physicians from other avenues. How could they help knowing this, from the often very acute observations they made of the course of the cancers they saw so plentifully? Now it is bolstered by many facts of mechanism unknown until recently. Not only are cancers unlike in the gross, but each cell in a cancer is an individual and differs from its neighbors—a fact unknown until microscopes were made, and then not until the cell doctrine was enunciated.

No two organisms are alike, is a first principle of biology and one of the starting points of the organismal philosophy. Pathologists have recognized this difference of one cell from another ever since they brought cancer tissue to the focal point of good lenses. The finer details which we now have of these differences give, in addition, an etiological slant. A good example is in the ascites tumors of mice, which have been more intensively studied during the past few years. Hauschka, in our Institutes, has counted chromosomes in the cells of a number of different ascites tumors. Klein, Levan, naturally find diploidy, but also euploidy, tetraploidy, heteroploidy, even 2,000 chromosomes, in the various cells. Etiologically speaking, Hauschka finds that ascites tumor cells with the normal mouse diploid chromosome count of 40 cells can be transplanted only into the very strain from which they came, or even into only the same family of the strain; whereas cells with heteroploid numbers of chromosomes can be transplanted successfully into various genetically foreign strains of mice. There is a definite correlation between chromosome constitution and antigenicity, and the fluctuation in chromosomal numbers allows the assumption that fluctuations can occur in all characteristics controlled by genes, including fluctuations in susceptibility and resistance to chemotherapeutic agents.

On first thought, there seems point in arguing that if we reach down deep enough into cancer cell physiology we should be able to plan a compound or compounds to destroy it, without unduly damaging normal cells. But there are few starting places, and at present more refined knowledge needs be obtained if by "digging down" we mean into life processes themselves, such as oxidation, reduction, absorption and utilization of building- and energy-producing-blocks. We may use trial and error methods such as many are attempting, and from which much useful information has emerged not only in the way of compounds but also in basic information. But to really plan chemotherapeutic substances requires more discoveries. The facts remain that,

biologically and descriptively speaking, the chief differences between cancer cells and corresponding normal cells are the distorted differentiation and the absent organization, processes which we may well believe have been added to normal cell behavior as superstructures in evolution. Not the general but what parts account for the above-mentioned special properties must be known in both normal and cancer cells for chemotherapeutic, diagnostic and other purposes, rather than the more basic activities of breathing, eating, digesting and excreting.

As an example of the biological approach to more details of cell differentiation and tissue morphogenesis, I cite the work of Briggs. With King he has developed micro-surgical technics to the perfection of transplanting nuclei from one cell to another. This is the only way known at present to answer the central question—what are the relative roles of nucleus and cytoplasm in cell differentiation?

So far, Briggs and King have succeeded in transplanting nuclei from undifferentiated embryonic cells into enucleated eggs. The transplanted nuclei are undamaged, go through a normal series of mitoses and give rise, in combination with the recipient cytoplasm, to normal complete embryos. The main question now is: "What will happen when nuclei of differentiated or cancer cells are similarly transplanted?" If the special characteristics of the differentiated and/or cancer cells reside in nuclei, it should be possible to detect such nuclear control by these transplantation experiments.

I could mention other examples, such as from genetics, in which nucleic acids and nucleoproteins are being pursued for their effects in special cell behavior. I dare to say that the processes under the biological names of differentiation and organization are the ones toward which translation into chemical terms needs to be done for rational planning of chemotherapeutic substances. The complications are many, among them the difficulties of obtaining cancer tissue free of stroma, wandering cells, and other extraneous material; and the difficulties of choosing control tissue which must not be completely differentiated nor organized. Here are some of the chemical differences thus far found. Cancer has more water and less calcium in it. Cancer has a high glucolysis and produces more lactic acid. Most of the known enzymes are less active and in smaller amounts, i.e. the "spectrum" of enzymes is less diversified among various cancers than the various normal tissues. The distribution of free amino acids is more similar among cancers than among different normal tissues. The B vitamins are less in amounts in cancer, except folic acid which may be higher, though this latter is disputed. There is a lower catalase value and a lower content of cytochrome pigments. The myosin fraction of normal muscle yields a different electrophoretic pattern than that of the myosin in rhabdomyosarcoma. There are more nucleic acids in certain cancer tissues. Were it not that considerable of these chemical data still need confirmation, it would be a sound theoretical starting point. Actually, a number of antimetabolites have been synthesized with the above findings in mind, even though many results have come from individual tumors and the findings in any and all cases remain to be explained in functional terms.

To return to a bit of history: During the course of the centuries innumerable theories of cancer were projected and, naturally, every theory of cancer gave rise to a therapy. When black bile was considered the cause of cancer, the black bile had to be eliminated and various means were used—however empiric and useless—to this end.

At other times it was considered a parasitic growth, as indeed many so consider it today. As with other parasites, it must be destroyed. At the time of the lymph theory, bad lymph must be eliminated, and this was done by drilling openings into cancers and allowing the material to drain out from the cancer and from regions removed from the actual site of the cancer.

Celsus (30 B.C.–38 A.D.) was a localist

and, therefore, stated: "we must find substances which differentiate between healthy and diseased tissue"—a discovery which today would be of the utmost value.

While not specifically intending to mention external remedies, nevertheless, in passing, it is of interest to note that among others of today, Mohs of Wisconsin, operating slowly and deliberately on external cancers, applies zinc salts in the attempt to distinguish between cancerous and healthy tissues. He has at his command the technic of preparing frozen sections during operation and the knowledge of reconstructive surgery.

Galen (131–203 A.D.), believing that cancer had a constitutional basis, gave purgatives of many kinds, and insisted on a special diet. Blood-letting and the use of ferric chloride locally were secondary treatments. This premise held for many hundreds of years. In the hands of some the constitutional treatment was primary; and in the hands of others the local treatment was of first importance with, however, attention to the diathesis. External treatments consisted of a vast variety of salves, plasters and caustics, which were divided into softeners, healers and extirpators. Among the remedies used both externally and internally which have persisted for years, we mention arsenic in its various forms. Today arsenic is still used, and all of us remember that Fowler's solution, starting with two drops per day, going to 10 or 15 drops and then being reduced, was and still is, one of the standard remedies for leukemia. Lead is another, and many of us remember Bell's use of lead some 20-odd years ago. There is no doubt of the influence of both arsenic and lead on various phases of cellular behavior, but they are not specific and they certainly are toxic.

This may be the place to mention that a number of remedies used against cancer also produce cancer, arsenic among them, to which may be added x-rays, some of the carcinogens and, I say, with my tongue in my cheek,—perhaps the estrogens.

When Paracelsus (1493–1541 A.D.), started the upset of Galen's teachings, he propounded the theory that cancer was due to a mineral salt (Sal. calcatharianum acutum), in the blood trying to get out. He was a local theorist. In addition to much alchemy and mysticism he introduced in the raw the idea "similia similibus curantur"—form opposed to form, snakes against snake bites, and cancer against cancer. He was not the first by any means to use cooked and uncooked crabs, crayfish, lobsters—locally and taken by mouth. A not uncommon remedy from the old Greeks was the ashes of crabs applied locally and administered in various forms. For cancer of the breast, crab soup was made with asses' milk, and this remedy was used even into the 19th century.

It is also interesting that when these and hundreds of other remedies did not cure a cancer, the chief value assigned to them was that they "relieved pain." Where have we heard this before? . . . and I wonder how often we will hear this in the next years? Not that I oppose the relief of pain—but it is so non-specific of a cancer remedy to diminish pain without removing the cancer. The relief of pain is a part, and a very important one, of what can be called "the general care of the cancer patient"—a subject on which I have spoken and written for many years. Big dividends are paid by careful attention to nutrition, digestion, rest, sleep, ventilation, recreation, blood picture, kidney function and, most important, the mental attitude of the patients and their relatives. With or without chemotherapeutic trials, neglect of the patient as a whole often leads to more intense and earlier tragedies than need be.

Most of the chemotherapeutic substances under trial today have undesirable side effects; for example, the nitrogen mustards destroy bone marrow, an evil to be anticipated and minimized where possible. Besides, many patients do not die directly of cancer in the sense that sufficient of vital organs are replaced by tumor. Fifty per cent or more of patients with carcinoma of the uterus die of uremia from obstruction of the ureters. Patients

with cancer of the tongue and mouth generally die of hemorrhage and/or sepsis—at least combatable processes.

Practically all patients undergoing trial with chemotherapeutic agents are in stages beyond surgical or irradiation help. Not all such patients are suitable for trial. The criteria must be: (1) is there a possibility of help, and (2) can something be learned? It is no easy task to say "No" to a patient, cachectic, anemic, with a liver full of palpable nodules, who looks for the last possible chance after a build-up of hope. And for the patient chosen there must be mutual sympathetic understanding of the situation. No guarantees, of course, but it is permissible, in fact essential, to hold out a trifle of hope—if not for "cure," at least for relief and prolongation of life. "Perhaps something better will appear in a month or two, or a year. Who knows what will be discovered next week?" The desire to be of help to others by contributing knowledge is an important part of the thinking of many patients, a fact which helps maintain confidence in the innate goodness of individual human beings. Permission having been obtained from the patient and/or the relatives (for in some cases the patient does not know the situation), evaluation of therapeutic effectiveness begins.

There are subjective and objective criteria; the latter can be made quite definite, the former are apt to be hazy and equivocal. How we all wish for a thousand cases of the same tumor in the same situation, the same stage, in patients of the same sex, same age, same state of nutrition, same mental make-up, same surroundings, etc., etc.! Or for a substance given by mouth or parenterally which would cause the tumor to steadily diminish, finally disappear, and stay away! Since such a remedy is not at hand, we are subject to the innumerable "perhapses" that we know, and to many of which we are ignorant. All of us are so constituted that when a patient says the pain is less or is gone, and states "I feel much better," and even when we observe objectively slight regression or cessation of growth, we are apt to attribute it to our method of treatment. An old saying insists that "we cannot be enthusiastic if we see all sides of a question." And we must be enthusiastic, or at least hopeful, in this field of hard work and many disappointments. We must be enthusiastic over gains, however submicroscopic, for without trial, no progress.

We do remember that a few cancers have disappeared "spontaneously," but so few that they are negligible for practical purposes. We should also remember that some untreated cancers grow slowly, take even ten years to kill; that there are spurts of growth with quiescence between in many; that our knowledge of the natural history of untreated cancer is too sketchy for statistical comparison. Life is short, art is long, and science a set of statistical probabilities. We should base our judgment on the most objective evidence possible.

Leads for evaluation and elaboration of chemotherapeutic ideas come from many sources, such as various scientific disciplines, enthusiastic engineers, chemists, biologists, physicists and others—excellent in their own fields but usually without sufficient knowledge of cancer—and then from the general public. In our Institutes we average about two cancer "cures" a week. Obviously, they cannot all be tried, so we have adopted a set of rules. We give our own findings and ideas first position, but occasionally we, as well as all others in the field, must give way to pressure—and this is what we ask:

1. We must be supplied with enough information about the general nature, method of preparation, details of previous tests, etc. of all compounds submitted to us, before any tests will be considered.

2. If the ideas behind the project seem reasonable, and the above qualifications are met, preliminary trials on mouse tumors will be made as soon as such experiments can be handled.

3. If the substances show promise we will consider further studies, after receipt of com-

plete information on the process of preparation and purification.

4. We shall undertake no clinical trials of any substance until thorough studies with animals have been made in *our* Institutes.

5. All data obtained on the material shall be released, under the sponsorship of our Institutes, only through publication in recognized scientific journals. Due credit will be given to the person submitting the ideas and material.

But it is time to come to specificities. The substances used in chemotherapeutic attempts may be divided into several classes. One, the antimetabolites—which are designed to poison particular kinds of cells, (in many respects these are the most interesting developments); two, the hormones; and three, the universal poisons.

In general terms there are two overlapping kinds of antimetabolites—the compound ones and the enzyme ones. The compound ones are those in which modifications are made of a normally occurring metabolite. Thus, in place of the methyl group in methionine, the ethyl group is substituted, resulting in ethionine. Crudely put, the theory is that such near relatives of normal compounds interfere with the absorption into the cells of normal compounds; or, having entered the cell, they prevent the formation of normal cellular constituents; or if the normal synthesizing enzymes within the cell are not too specific they are synthesized with the formation of a strange compound which the analyzing enzymes within the cell cannot break down. Thus a monkey wrench is thrown into the machinery of the cell and the cell perishes.

In the case of ethionine, it has been found by isotope tracer technic that it does, indeed, enter the cell and is synthesized within a protein molecule (Stekol). The protein, now containing ethionine instead of methionine, presumably cannot be metabolized, and thus the machinery stops.

A similar line of reasoning, however crude, can be applied to other substances such as the pyrimidine and purine analogs. Unfortunately, as stated, not enough is known of substances peculiar to cancer cells, so the trial and error method of making many compounds must be pursued. Fortunately, in experimenting with such compounds considerable knowledge is gained of normal cell metabolism.

In enzyme antimetabolite studies a strange precursor is administered, resulting, theoretically at least, in a strange combination within cells which again disturbs normal metabolism.

The most widely tried of the antimetabolites are the relatives of folic acid. Beginning with diopterin, containing two glutamic acid groups, then going to teropterin with three, other compounds with many glutamic acid groups attached to the pteroyl nucleus have been synthesized. A number of case reports have accumulated. Occasionally, shall we call it an interesting result, has been obtained in human beings, although animal experimentation has proved negative.

Another amino acid, namely, aspartic acid, has been attached to the pteroyl nucleus with no particular advantage, but when an amino group is inserted results in the right direction appeared with, for example, aminopterin. This highly poisonous substance has found its greatest usefulness in acute leukemia, especially in children. At times it produces complete remission for a number of weeks or months. At other times it will transform an acute leukemia into one of the chronic varieties which give better opportunity for further treatment. In some cases, naturally enough, it has no effect. In none has it been curative.

Other substances containing the amino group, such as A-methopterin, produce essentially the same results but less consistently. The advantage is a greater span between effectiveness and toxicity. They have been of little value in other conditions, except for an occasional help in the lymphatic tumors.

Several years ago, while we were using teropterin and the amino acid-containing antifolics, Dr. Toennies of our Institutes became interested in the folic acid content of the blood, with a view to more rationally chosen dosage. These determinations proved

to be extremely difficult, and before long it was found that nothing short of a full-fledged research program on folic acid and folic acid-like substances would give the information needed. Toennies is proceeding with such work. Perhaps, in addition, it will throw light on folic acid, B_{12} and other substances as they influence butter yellow carcinogenesis—a field in which Dr. Bennett and Dr. Sorof of the Institutes are heavily engaged.

In brief, the values of folic acid in the blood of normals, those with cancer and those with other diseases, were scattered very widely, so that no generalization is possible.

The general inconsistencies in clinical results with antifolic compounds may be partly explained by the previously mentioned variations among cancer cells, in addition to what seem vagaries in folic acid metabolism. Indeed, Law of the National Cancer Institute found that the leukemia cells of mice could be divided into susceptible, resistant and, most intriguing, into those dependent on the antifolic substances. Undoubtedly, the effect of an antimetabolite depends on the metabolic pattern of the cells to be influenced, and these results of Law show that cells even in the same type of cancer can vary in their metabolic behavior. Thus we can understand better the conflicting results obtained when different types of tumors are treated, not only with antifolics but with many other analogs.

Among various other metabolites could be mentioned guanazola, but the results thus far simply indicate that there is a wealth of more experiments remaining to be done. Indeed, a metabolic block from internal causes, without the addition of an extraneous substance, can force normal substances to be antimetabolites.

Experience with hormones as chemotherapeutic agents has been long and varied. When irradiation of the ovaries following radical breast amputation became the vogue around 1925, Dr. John B. Deaver told us that early in the century he had removed both ovaries from a number of patients following radical amputation of the breast for carcinoma. He also stated that Warren of Boston had suggested this some years before. Dr. Deaver abandoned the procedure because he did not see better results than from uncomplicated radical amputation of the breast. Renewal of interest appeared some twenty years later, and there seems little doubt that a few cases, especially in younger women, were benefited by irradiation of both ovaries, although there was much debate as to final results.

With increase of knowledge of sex hormones in general, and with the advent of chemically pure estrogens and androgens, more controlled observations were possible of sex gland relationships. Since there is debate as to the kinds to be used, the dosage, time intervals, and other such pertinent questions, it is perhaps unfair to generalize, but if principles are wanted we can summarize our practice and experience.

At first the general rule was adopted of using testosterone in women under 50 and estrogens in those older, but comparison of results with those of others gradually led us to use testosterone in most of the older patients as well. From administering either estrogens or androgens in patients with fairly advanced metastases, we now are seeing patients as soon as metastases become evident. The disadvantages of testosterone are masculinization, with the development of beard and mustache, general hypertrichosis, change in psyche, alteration in protein and salt metabolism, etc. The results consist of apparent cessation of growth of metastases to actual disappearance of many and, when present in the bones, to recalcification.

About two years ago a testosterone preparation from which the masculinizing effect had been partially removed was offered for use. Our experience bears out the less masculinizing influence, but we have been compelled to increase the dosage for results and thus, in the end, the masculinizing influence was again present. For the past six months we have been using a depot-type of testosterone in a dosage of 400 mgs. given hypodermically once every two weeks. In any case it has been our experi-

ence that the usual dosage recommended is not sufficient. Of ordinary testosterone we use 100 to 150 mgs. three times a week.

The patient we use as an example is a 47 year old woman who had a radical amputation of the left breast performed three years ago. About two years later she complained of severe backache, loss of weight, and general malaise. She had metastases in various parts, but particularly marked destruction of the left ilium with erosion of the upper part of the left femur and the right ilium. Five months after beginning treatment there was healing in both ilia and the left femur. Irradiation was also given to the major area of the left ilium, and six months later, i.e. approximately one year after beginning of treatment, there was healing in both ilia and femur. She received Methostan, a testosterone preparation in less masculinizing form, for the first six months, and now is receiving depot-testosterone. Her symptoms have largely disappeared, she is able to do her housework without difficulty, has gained weight, and feels in good health at the present writing—approximately 15 months after beginning of testosterone administration. She has a minimum of masculinization.

In every case of ours in which testosterone has produced results growth of the tumor was resumed and new metastases appeared sooner or later—sometimes in six months, sometimes in 18 months or longer. Such patients are then placed upon large doses of estrogen, but with only an occasional result. Our experience with estrogens dictates the use of testosterone from the very beginning in most cases.

Our results with hormones in carcinoma of the uterus and of the ovaries parallels that of others, i.e. they have been negligible. We have used the estrogens, progestin, testosterone in large doses in the papillary types of carcinoma of the ovary with peritoneal implantation, and have watched tumors grow with undiminished energy. Irradiation has also failed.

The story of carcinoma of the prostate gland is more favorable. Following Huggins' lead, bilateral orchidectomy is practically a standard operation. A theoretical base can be set up as follows: We argued that testicular secretion is necessary not only to initiate but to maintain differentiation of the cells of the normal prostate. Acid phosphatase produced by these cells is one of the products of the activity of tiny laboratories within prostatic cells as an expression of their differentiation. Castration in normal men results in atrophy of the differentiated cells lining the acini of the prostate; castration before puberty leaves the prostate in its infantile stage without differentiation of its acini and the lining cells. So, if a cancer of the prostate has fairly well differentiated cells, bilateral orchidectomy, removing testicular secretion essential for the maintenance of differentiation, leads to disappearance of the cancer cells which have differentiated. Thus the size of the tumor is diminished. By this same reasoning, it was argued that cancers composed of undifferentiated cells would not respond to bilateral orchidectomy as would the others. Roughly, this theory has been borne out and the best results from bilateral orchidectomy may be expected in the adenocarcinomas of the prostate and their metastases. Well differentiated cells can no longer divide, and since the cancers of the prostate, no matter how well the cellular differentiation, do continue to grow—they must contain some undifferentiated cells which will not be prevented from multiplying by bilateral orchidectomy. We can therefore expect redevelopment of nodules from small foci in the original metastatic nodules, from cells which have not undergone dissolution.

A similar line of reasoning applies to the use of female sex hormones in prostatic cancer, but they must be given in sufficient dosage to overwhelm testicular secretion if the testes are allowed to remain—and perhaps they help neutralize androsterones from the adrenals.

Several years ago Huggins began performing bilateral adrenalectomies—in patients with recurrences of previously disappeared metastases. His results warranted continuing the procedure. This is possible by the advent of substitution therapy in the form of cortisone,

desoxycorticosterone, and knowledge of potassium balance.

As an example of the above arguments and of the benefits of bilateral adrenalectomy, the following case is presented:

A 68 year old man complained of pain in the lower back region and was found to have cancer of the prostate with erosion of the lower ramus of the right pubic bone. Bilateral orchidectomy was performed. Three months afterward there was healing of the bone; estrogen therapy in the form of diethylstilbesterol, 5 mgs. per day, was also given. Two years later his disease began afresh. Estrogens were continued, plus irradiation. Again there was erosion of the ramus of the right pubic bone, and a mass was felt in the right side of the pelvis. Bilateral adrenalectomy was then performed. Four months later there was beginning of healing of the bone and the mass began to disappear. About four months later, i.e. eight months after the bilateral adrenalectomy, the lesions in the pubic bones had healed and the mass had disappeared completely. The last radiograms were taken one month ago. The patient continues in good health, has gained weight, has retired from his business as draftsman, but works around his home and is looking forward to planting his garden this spring. As in most cases, the acid phosphatase levels in his blood returned to normal within a week, thus antedating radiological evidence of regression and again confirming the sensitivity of this test. Would that we had a similarly sensitive test for every cancer!

As in all of the other subjects brought up, there are enough data for several hours for each subject, but this must be sufficient for our present purpose.

Among the poisons, we mention the nitrogen mustards. Their usefulness lies chiefly in the various lymphomas, including Hodgkin's Disease, some cases of leukemia and an occasional case of carcinoma of the lung. They are given intravenously in doses of 1 to 3 mgs. for three or four doses, at intervals of from five days to two weeks. Their administration in favorable cases is followed by diminution of the size of enlarged lymph nodes, by reduction or abolition of fever, and a sensation of feeling better. Unfortunately they damage the bone marrow and careful, oft-repeated blood counts must be made. The bone marrow frequently recovers promptly, but in some cases the damage is long-lasting. They should not be used when the hemoglobin value is 60% or below and/or the red count is 3,000,000 cells per cubic millimeter or less. By intra-arterial catheter, nitrogen mustard and a few other substances have been injected directly into tumor areas, resulting in necrosis.

A synergism between the mustards and irradiation has been noted, in the sense that when patients, for example, with lymphosarcoma, become radiation resistant—as many if not most of them do after variable periods of time—a course of nitrogen mustards, followed by irradiation if the mustard alone does not cause satisfactory regression, will result in restoration of radiation sensitivity and thus prolongation of life in fair comfort. By radiation sensitivity is meant sensitivity to gamma irradiation. This interesting synergism is difficult to explain; on practical grounds it seems reasonable that cellular damage produced by any agent will increase sensitivity to further chemical changes induced by ionizing radiations.

The nitrogen mustards occasionally restore sensitivity also in leukemia which has become insensitive. This phenomenon is interesting inasmuch as many other substances produce the same effect, for example large intravenous doses of typhoid vaccine. After the chills, fever and shock subside, sensitivity is often restored.

But the substances which I would like to mention more specifically are the ones in which we have had most experience and which have been our "pets" so to speak. These are the polysaccharides. Their history is a long one, beginning with the observation that now and again a patient's malignant tumor regressed in part or completely after attacks of erysipelas. In the majority of cases the

patients, if and when they recovered from erysipelas, went on to die of their malignancies, but every now and again a tumor disappeared in just enough cases to maintain interest.

In 1896 a young resident surgeon in New York observed a patient with lymphosarcoma who had wide-spread disease after a number of operations. The patient developed recurrent erysipelas, whereupon the tumor disappeared and the man remained free of the malignancy for some 30 years. This made a deep impression upon William B. Coley, who began experimenting with various preparations and remained intensively interested during the rest of his life.

At first he used *S. erysipelatus*. Later it was discovered that *Bacillus prodigiosus*, now usually called *Serratia marcescens*, increased the virulence of streptococci when the two were grown together, so Coley produced a mixture of Streptococcus and prodigiosus, and this became known as Coley's Toxin or Coley's Fluid during the course of the years. No doubt thousands of cases were given Coley's Fluid with no results, but both here and abroad, every once in a while, the desired effect was noted and this was sufficient to maintain not only the interest of Coley but of others as well.

Coley's daughter, Helen Coley Nauts, at the cost of much labor, collected many case histories. There are some 500 authenticated cases in which the use of Coley's Fluid caused definite regression and in a number of cases "cures." In the light of our present knowledge, we may explain why the preparations produced by particular bacteriologists, such as Park of New York, Martha Tracy of Philadelphia and others, varied in potency. When placed on the market by a commercial drug house still further variations occurred, since the heat sterilization destroyed much of the activity of the toxins. It must be remembered that much of the work was done before tumor mice were available, so that the preparations were tested for toxicity and sterility but could not be tested for potency except on the patients themselves. The introduction of animal tumors of well studied kinds, such as Sarcoma 37 in mice, added another tool, so that potency also could be tested.

Shortly after the end of the first war, Murray Shear, arguing that there must be some active substance in the witches' brew of killed streptococci, prodigiosus and broth, began fractionation. He discovered an "active' principle in a polysaccharide fraction. The test animal in this work was the mouse bearing Sarcoma 37, and hemorrhage and necrosis were found in the sarcoma within a few hours after injection of a potent polysaccharide with a minimum in other parts of the mouse. Cautious trials were made in patients by Shear and Brues, with results that encouraged further work. Shortly afterward Shear very kindly offered to provide us with his polysaccharide fraction. Trials again gave sufficiently encouraging results to warrant further exploration. The disadvantages were toxicity and antigenicity, but there was no doubt that hemorrhage and necrosis occurred in human tumors. Coley found most of the favorable results in sarcomas, but occasionally a carcinoma also responded.

Dr. Hugh J. Creech joined the Institutes at this time and began attempts to reduce toxicity and antigenicity and still retain the tumor-destroying powers of the polysaccharides. Beginning with the preparation from Shear which he called P-3, a great variety of methods have been used by Dr. Creech and his associates, to prepare well over 100 fractions. Most of them were no better than the original P-3, as evidenced in mice, but among them a few better preparations have appeared. After due animal experimentation for toxicity, antigenicity and potency, they were cautiously tried in human beings.

The polysaccharide is a huge molecule or perhaps a number of large molecules combined like polymers as in rubber. Some fractions contain a higher nitrogen content, others a lesser, with little difference in potency but differences in toxicity and antigenicity. In the molecule are a lipid complex, a phosphorus linkage to the lipid moiety and the carbohy-

drate part. The molecular weight is around eight million. Electrophoretic patterns are fairly homogeneous in some fractions. The source of the polysaccharides is *Serratia marcescens* cultured in a simple medium containing inorganic salts and glucose.

Highly potent tumor-destroying polysaccharides have been isolated also from *E. coli*. Fractions produced from Staphylococcus and Streptococcus have been found inactive. Parenthetically, difficulty was experienced in obtaining a culture of Streptococcus from a case of erysipelas untreated with antibiotics, and over a period of two years only one such case was encountered, and the material obtained from it was inactive. As a matter of interest, requests were made to various parts of the world, such as India, asking for cultures of Streptococcus from untreated cases of erysipelas. Answers were received from our friends—sometimes written in an indignant mood, asking, what did we think? . . . that they were so far behind that they did not treat erysipelas with penicillin or some other antibiotic? Apparently many physicians in various parts of Asia have not seen a case of erysipelas in years.

Tests for antigenicity have been made by precipitin, agglutination and complement fixing reactions on sera of rabbits, mice and human beings. The preparations vary in their antigenicity. Interestingly enough, tolerance appears within 24 hours, but there is wide variation in agglutinin and precipitin titers from case to case, and in their times of appearance. An immune serum obtained from rabbits passively protects mice against lethal doses of the polysaccharides, but this has not been carried over into human beings, for obvious reasons.

The development of antibodies in human beings, we believe, damps down if not completely stops the tumor-destroying activities of subsequent doses. Therefore, in most patients it has been our practice to give as high a dose as possible for the first administration. Subsequent doses are now given at intervals of not less than two weeks apart, since the antibody levels are reduced appreciably in that length of time. The amounts of antibodies produced in animals and in patients are not sufficiently high, however, to increase the levels of gamma globulin to an extent detectable by electrophoresis.

The dose of P-5 used in human beings was of the order of 10 micrograms given intravenously. Temperature begins to rise in from one-half to three-quarters of an hour, reaching a peak of 105° in about two hours. This is accompanied by severe chills and fall in blood pressure to a systolic figure of 70. Fever slowly subsides, blood pressure slowly rises, and in most patients recovery is complete in 24 hours. During the height of the reaction there is often nausea and vomiting, backache and, most intriguing, in many patients pain and swelling in their tumors. In many instances, tumors on or near the surface of the body showed ecchymosis. The latter is of more than passing interest and in a number of cases acted as a guide to surgeons. As an example, a patient with fibrosarcoma, partially removed a number of times over a period of two years, presented a vaguely outlined infiltration of the upper part of the thigh. According to usual practice a biopsy was taken before and three days after administration of P-5. The tumor, from being vaguely outlined, now stood out swollen and demarcated by ecchymosis. The surgeon removed a piece for biopsy and then decided he could tell where the tumor ended and healthy tissue began, so he continued his operation and removed large masses. This patient is not cured and subsequently had a number of polysaccharide administrations along with operative procedures. He is still living and carrying on his usual activities—seven years after his original admission.

With the advent of ACTH and cortisone it was thought that a means of damping down immune reactions was at hand, and for a time cortisone was used routinely in methods worked out by Dr. Thomas C. Pomeroy. Experience with ACTH resulted in near disaster in several patients and its use was immediately discontinued. We theorized about this, but too

many questions await answers for us to be certain our theories suffice. Experiments with mice indicate that if cortisone is given before the administration of polysaccharides less hemorrhage and necrosis occur in the tumors, so a routine was worked out whereby cortisone in approximately 150 mg. doses is given to patients beginning about three hours after polysaccharides are administered. To our satisfaction, it was found that cortisone acts as a support for the patient in the quasi-shock which occurs. Further studies are being done to see if cortisone will damp down the production of antibodies and thus allow further doses of polysaccharide to be effective.

Our present preparations, which we call MP-30 and MP-50 are not only less toxic to mice and human beings, and therefore can be given in larger doses, but with the help of cortisone another boost could be given in the size of the dose. In fact, at the present time, 100 or more times the dose of P-3 is used. I pay tribute to Dr. Creech and his associates in their endeavors to reduce toxicity and antigenicity and at the same time retain tumor-destroying properties.

More recent experimental observations of tumor metastasis have revealed that cortisone enhances metastasis of tumors in mice, and in a few instances may have played some part in the spread of tumor in patients, although this latter cannot definitely be proved. At any rate, the danger of such a phenomenon in human beings has caused us to abandon the routine use of cortisone until the situation is clarified. It is apparent that these findings should also be a warning against the further widespread empiric use of cortisone and ACTH for the production of a sense of well-being in cancer patients.

Naturally, other supportive treatment is given such as glucose and saline solutions, blood and/or plasma transfusions, sedatives, and others. All of our patients have advanced malignancy and many spend a week or more in preparation for their ordeal—and no less word can be used to describe it. However, it is of short duration, in contrast to some other chemotherapeutic agents in which damage to organ systems is wide-spread and long-lasting. There is a fall in the number of platelets with a prolonged prothrombin time during polysaccharide administration which lasts for about two weeks and which is another factor in choosing a treatment interval of two weeks or more. There is no particular diminution in red cell count. The leukocytosis is also of short duration.

From the above remarks it is apparent that closely timed teamwork is necessary in the administration of the polysaccharides. Of the many questions, such as means of measuring the dissolution of tumors other than through observation, such as by changes in uric acid and purine excretion in the urine, all require much further investigation.

The addition of polysaccharides to tissue cultures results in no obvious destruction. Determinations in the Warburg apparatus of oxygen and carbon dioxide exchange of tumor and other tissues mixed with polysaccharides, results in no change. However, tumor tissue removed from a mouse which has had previous injections of polysaccharides shows a distinct difference from controls. This leads to the assumption that polysaccharides do not act directly, as such, on the tumors, but that some metabolic conversion or interconversion takes place and, shall we call them "intermediates," are the potent substances. This again is a stimulus for further work but we have dozens of questions in our notebooks requiring thousands of mice, and who knows how many hours of time in the laboratory? Our final word this evening is that results, especially in sarcomas (except malignant melanomas) are a trifle better than they were several years ago.

Finally, I mention isotopes. When they were first heralded in the public press particularly, great hopes were given that they would be the answer to at least part of the cancer problem. Results, generally speaking, have been disappointing. P^{32} was used in the treat-

ment of leukemia for several years. Most workers found that there were no real advantages over good, externally delivered irradiation. The problem still remains, however, of cataloging differences, if there are any, between irradiation delivered from outside and that delivered from within cells, assuming, that the cells absorb the P^{32}.

In polycythemia vera, P^{32} has proved of great help, and we might cite several cases. Its use can be recommended in this condition.

I^{131} is used in carcinoma of the thyroid with occasional beneficial results. In this case also, the degree of differentiation of cells in the tumor determines whether they have within them the necessary laboratories which will pick up the I^{131} when it is administered. Only adenocarcinomas respond.

In addition to treatment, I^{131} is of help in determining the presence and position of metastases in adenocarcinoma of the thyroid. Thus, in so-called metastasizing adenomas (Virchow's term and a poor one), the Geiger counter will demonstrate metastases, for example, in the tibia.

Of the other isotopes under experiment, such as radioactive gallium and others, we must await further information from the laboratories especially set up for this exacting work.

Radioactive gold has proved of considerable value in one particular situation—namely, pleural effusion and ascites from metastatic tumors. The rate of reaccumulation of fluid is slowed down, and our experience in several cases has been that it, possibly by production of adhesions, has permenently halted fluid accumulation.

And now I hope that I have justified, even to the most conservative, the title of this presentation—"A Report on Microscopic Progress in the Chemotherapy of Cancer." To the enthusiast, perhaps it should have received a more daring one. At least when we are asked, as we so frequently are, "Is there progress being made?", we can say "Yes."

Medical Students and Their Examiners in Eighteenth Century America*

By WHITFIELD J. BELL, Jr., PH.D.

Professor of American History, Dickinson College, Carlisle, Pa.

UNTIL the nineteenth century practically all the physicians in the British American colonies and the United States were men without formal qualifications for practice. They had heard no lectures, performed no experiments, and, more than likely, seen no dissections. They called themselves "Doctor" not because they were graduates of a university, with a diploma to show, but because they were in fact practicing what doctors of a university usually did. As apprentices to an older man, they had observed his methods of treatment, prepared his medicines, and read his books for a year or two until, with only his certificate recommending them to those who might need their services, they moved out to practice on their own.

Such methods of instruction and qualification dismayed and angered that generation of high-minded young Americans who went abroad to study medicine during the third quarter of the century and returned home to give medical education and practice new foundations and new directions. The Virginians at Edinburgh in 1761 or 1762, for example, formally petitioned the Virginia Council and House of Burgesses to take measures to "prevent any one for the future from professedly practicing medicine who had not received a public testimony of his abilities, by being properly licensed and honored with a doctor's degree." When nothing came of this proposal, a few years later another suggestion with the same end in view was submitted informally to Richard Henry Lee by his brother Arthur, one of the medical Virginians at Edinburgh.[1] In short, nothing was clearer to the Americans, as all their correspondence from Britain amply shows, than that, for the honor of their country and the safety of their fellow-citizens, medical practitioners must follow a formal course of professional instruction through several years and that their abilities must be tested by examination and sealed by the awarding of a diploma.

For most Americans in the middle of the eighteenth century Edinburgh was the principal seat of medical training. Medicine was taught better there than at Oxford, for example, where the sciences were moribund, or at Cambridge, where conditions were little better. For this reason alone students would flock to the northern university. Another reason was the practical one that Samuel Johnson gave Arthur Lee. At Oxford and Cambridge, Dr. Johnson told the Virginian, they never allowed students to begin physic until seven years of literary study had qualified them for the degree of master of arts. "Therefore," Johnson continued,

> if you have a large fortune and time enough to spare, go to either of these. If you would choose immediately to enter upon Physic and to attain sufficient knowledge therein to carry you through life, at a small expense and in a short time, by all means go to Edinburgh or Leyden; for the Scotch or foreign education is like a house built to last a man's lifetime only; the English is like a Palace or Fortress intended to last for many ages. The first build lightly, the last lay a very strong and firm foundation before they begin the work.[2]

* Read before the College of Physicians of Philadelphia's Section on Medical History, 29 January 1953.

[1] W. B. Blanton, *Medicine in Virginia in the Eighteenth Century* (Richmond, 1931), 401; "Early Letters of Arthur Lee," *Southern Literary Messenger*, XXIX (1859), 71–72.

[2] *Ibid.*, 62–63.

John Moultrie of South Carolina received the degree of doctor of medicine from Edinburgh in 1749. He was the first in a stream of Americans which continued until well into the nineteenth century. Before 1800 one hundred and fourteen received the honors of the University, and at least as many more studied there without qualifying for the degree.[3] "The American students, of which there is a great number," wrote Lee in 1761, "are in general well esteemed for their close application to their studies." More industrious than the Irish, who were said to revel extravagantly "in the public scenes of dissipation," living more genteely than the impecunious Scots, who were resolved to get as much learning as they could in the shortest time possible, the Americans were a self-conscious group, intensely proud of their American birth, eager and determined to do credit to their homeland.[4] The Edinburgh degree to them was the hallmark of professional competence and an earnest of successful practice in the future.

As soon as they reached England the Americans began to walk the wards of a great hospital like St. Thomas's and attend the anatomical lectures of the Hunters or Colin McKenzie. At Edinburgh they enrolled for the formal medical lectures, and sometimes for arts lectures in the College as well, and they attended the practice of the Royal Infirmary. Scrupulously, doggedly they copied whole volumes of notes, studied the medical classics and read the latest literature. In their rooms they sometimes dissected animals, and weekly in their student societies they discussed and debated medical ideas. At every stage they were guided by the advice of older students and especially by that of Dr. John Fothergill in London and Dr. William Cullen in Edinburgh. After two, three, sometimes more years of this, they were ready at last for the examinations which would admit them to the doctorate. All examinations were general, for none were given in particular courses.

EDINBURGH EXAMINATIONS

Samuel Bard of New York described them briefly in a letter to his father:

> The day before yesterday I was dub'd a Doct^r with all the form & Ceremony necessary upon the occasion. Doct^rs Monro senior & junior, with Doct^r Cullen, were in all my private Tryals my Examinators. My good Friend Doct^r Hope publickly impunged my Thesis. To all of them I consider myself as much obliged for their behaviour upon these occasions, in which, altho' they kept up the strickness of Professors, they never lost sight of the politeness of Gentlemen.
>
> The manner of my Examinations was as follows: on the first day I had not the most distant hint what was to be the subject of my Tryal, & went in trembling, & Doct^r Cullen, after desiring me to set down, began my Examination by asking me some general Definitions as Quid est medicina? & so on. They then askd me some questions upon the structure of the stomach & alimentary Canal, thence made a digression to the Diseases [of them], examined me upon the colic, Illius, their Diagnostick & method of Cure; then Doct^r Monro junior asked me the distinction between Illius & Inflammation, some physiological questions upon the Pulse in Inflammations, the causes of Intussusceptio in the Intestines, and the method of cure in both these Diseases. This ended my first Examination, which lasted about 45 minutes.
>
> My next Tryal was writing Commentary's upon two of Hippocrates aphorisms, and defending them against old Doct^r Monro & Doct^r Cullen, which took up one hour. My last private Tryal was writing commentary's upon two practical Cases (much in the same manner as that I sent, which I wrote for the medical society), which I defended against young Doct^r Monro & Cullen. This Examination took up an hour & a half. Lastly I was publickly in Hall to defend my Thesis. During all these Tryals, my Exercises were written in Latin, and I was obliged to defend them in the same language; not even in the first, where we are ignorant of our subject, are we allowed to speak a word of English.[5]

Students who had passed through such a curriculum and qualified by such tests under-

[3] *List of the Graduates in Medicine in the University of Edinburgh from MDCCV to MDCCCLXVI* (Edinburgh, 1867). From this Samuel Lewis extracted the names of the American students, which he published in the *New-England Historical and Genealogical Register*, XLII (1888), 159–165. W. J. Bell, Jr., "Some American Students of 'That Shining Oracle of Physic,' Dr. William Cullen of Edinburgh, 1755–1766," *Proceedings of the American Philosophical Society*, XCIV (1950), 275–281.

[4] "Early Letters of Arthur Lee," *loc. cit.*, 63–65; Edward Topham, *Letters from Edinburgh* (London, 1776), 209.

[5] Samuel Bard to his father, [May 1765], Bard Collection, New York Academy of Medicine.

standably had nothing but scorn for men who never took an M.D. or got one without working for it.

For in 1760 it was possible in many universities to obtain a doctor's degree easily. If Oxford and Cambridge required an abnormally long period of study, a few universities granted medical degrees in absentia, while others required a merely perfunctory examination. At Aberdeen, for example, a lively "traffic" in medical degrees was carried on. One might obtain a degree at St. Andrews on payment of the required fees and the presentation of two certificates of good character from medical men. George Glentworth of Philadelphia obtained his degree in this way. On the Continent an unambitious student might visit Rheims for a few days and, having paid a few pounds, depart a doctor of medicine.[6] Even at Edinburgh, where the professors guarded the reputation of their profession more jealously, it was not unknown in the eighteenth century for someone to get a degree without having attended lectures there.

Such an event occurred in 1764 when Edinburgh University granted the degree of M.D. to one Pultney. The regular students were incensed, for they believed the integrity of their own degrees was involved. Several Americans, notably Arthur Lee, seem to have taken a lead in making a public protest to the professors, "perhaps the only instance," Lee thought afterwards, "wherein students have remonstrated against the facility of their Professors, or ventured to oppose the proceedings of those who are to be the Examiners of their abilities." They acted, he explained, solely "with a view to maintain the dignity of the practice of medicine in Virginia."[7] Two years later the affair of Samuel Leeds called Scottish medical degrees into question once more.[8]

As a result of these incidents, in 1767 the University adopted regulations for the conferring of degrees.[9] No one might be admitted a candidate for a degree who had not completed a course of study in all the branches of medicine at Edinburgh or another university. When "some very young persons, quite lads," who had spent only a little time at the University, and that frivolously, and were not yet 21, were graduated in 1775, the older students protested,[10] with the result that the course of study was specified in 1777 to mean classes in anatomy and surgery, chemistry, botany, materia medica and pharmacy, theory and practice, and clinical lectures at the Royal Infirmary. In 1783 the course of study was fixed at three years, of which at least one must be spent at Edinburgh.

The new regulations of 1767 further required that three months before the date he expected to receive his degree the candidate must apply to the Dean of the College of Physicians of Edinburgh for private examination. This was a kind of qualifying examination which tested the student's literary attainments in general and his medical preparation in particular. It was held at the home of one of the professors, who, as his colleagues' host on the occasion, seems to have acted as chairman of the examiners. Students believed it made some difference to whose house they were directed: Monro secundus, for example, was thought to be "a very fair examiner." Should the student fail this examination, he must spend at least another year at Edinburgh—or go to St. Andrews and buy a degree.

[6] Betsy Copping Corner, *William Shippen, Jr. Pioneer in American Medical Education: A Biographical Essay* (Philadelphia, 1951), 42; D. M. Lyon, "A Student of 1765–70—A Glimpse of Eighteenth Century Medicine," *Edinburgh Medical Journal*, n.s., XLVIII (1941), 195.

[7] R. Hingston Fox, *Dr. John Fothergill and his Friends* (London, 1919), 145; "Early Letters of Arthur Lee," *loc. cit.*, 70.

[8] Fox, *op. cit.*, 74–78; Henry G. Graham, *Social Life of Scotland in the Eighteenth Century* (2v., London, 1900), II, 216n.

[9] Alexander Grant, *The Story of the University of Edinburgh during its First Three Hundred Years* (2v., London, 1884), I, 330–332.

[10] Basil Cozens-Hardy, ed., *The Diary of Sylas Neville, 1767–1788* (London, 1950), 217–218.

Sylas Neville, an Englishman, described his examination in 1775:

> Dr Home examined me on the circulation and the diseases of the skin. . . . Old Cullen took me next upon the insensible excretion or halitus from the lungs, catarrh, measles and the peripneumony, which is often the companion of that disease. He began by telling me that he was so well satisfied with the answers he had from me, that he did not think it necessary to ask me any further, but as it was the custom, etc. Dr. Black, who with Dr. Monro came in after the examination was begun, asked me concerning the influence of the excretions by perspiration and urine. Dr Hope then asked me the definition & symptoms of Diabetes. Dr. Monro asked me some questions concerning the cure of the same disease. Dr Home then desired me to retire a little, and in about half a minute being called in again, Dr Home told me after the specimen I had given of my erudition & knowledge in Medicine, the Faculty very willingly admitted me into the number of candidates.[11]

Now the candidate must submit his inaugural thesis to his professor to read, correct, and approve. Neville, it is interesting to note, selected his topic on June 18; he began writing on July 2 and gave Cullen an outline and partial draft on July 4; and completed the thesis by July 30. That the professor's approval was not given as a matter of course John Ravenscroft of Virginia testified. His first draft was returned to him for revision. "I'm like to greet [cry] about my Thesis," he complained,

> for Dr. Gregory to whom I had shown what I had wrote has set me to work so that I will be obliged in a manner to do it all over afresh and writing two or three times over 15 folio Pages is na sma Drink. It was so provoking when he was reading it over—he would hum and hah at every line and say, 'My Dear, this is not English,' 'This I don't understand' two or three times on every page, when I thought the sense clear enough and the meaning as plain as the Nose on his face. . . . [12]

Only now was the student admitted to his final examination. In the presence of the entire faculty in the University library he was examined searchingly by two members of the faculty appointed for the purpose. The examination might range over the whole field of medicine, including matter taken from any or all the prescribed courses. Neville, for example, was examined by Hope and Cullen on the subject of erysipelas. When he had answered these questions satisfactorily, the candidate received two aphorisms of Hippocrates to explain and two case histories to diagnose and prescribe for. These answers were to be written in Latin, the language in which all the examinations, oral as well as written, took place, and must be returned and defended within a specified time—usually between one and two weeks.

For the ordeal of the examinations, with their questions and answers in Latin, and their essays on Hippocrates and specific cases the students were in some degree prepared by the work of their medical societies. In these organizations—the Medical (now the Royal Medical) Society was oldest and best known—each student prepared in his turn a commentary on a Hippocratic aphorism, an essay on a medical question, and the diagnosis of a particular case. These he must present and defend before his fellow members. In this way the students discussed moot medical points, practiced their medical Latin, acquired some poise and self-confidence when speaking before a group—all good preparation for the University's formal medical examinations at the end of the course. Of Americans not fewer than 20 were members of the Medical Society in the period 1755–66 alone.[13]

Only now, when these written exercises were completed, was the thesis printed and a copy delivered to each of the medical professors. On the day of graduation the candidate must appear once more in public, this time to defend his thesis. Although this appears to have been largely formal, the students faced their questioners nervously. The candidates then retired, the faculty voted the degrees,

[11] *Ibid.*, 218.

[12] Lyon, *loc. cit.*, 197.

[13] James Gray, *History of the Royal Medical Society, 1737–1937* (Edinburgh, 1952), 25–64, 73–74; Samuel Bard to his father, September 1763, Bard Collection, New York Academy of Medicine.

and the students returned to be formally invested as doctors of the University.

PHILADELPHIA EXAMINATIONS

Examination practices at Philadelphia, New York and Cambridge in the eighteenth century were similar to those of Edinburgh in some respects, simpler in others; while the original regulations of the College of Philadelphia appear to have drawn elements from both the Scottish and English universities.[14] There was even a student medical society at Philadelphia whose exercises afforded practice in answering the kind of questions the professors asked.

The regulations adopted at Philadelphia in 1767 provided for two degrees—the bachelor's and the doctor's.[15] The general requirements for the degree of bachelor of medicine were three. In the first place, the candidate must have a knowledge of Latin and such branches of mathematics and natural philosophy as were deemed necessary for medical studies. Graduation from a college was presumed to assure such competency; other students must submit to an examination, but the College provided a course in natural philosophy for medical students. Secondly, each student must have attended at least one course of lectures on anatomy, materia medica, chemistry, and theory and practice, and one course of clinical lectures, and have attended the practice of the Pennsylvania Hospital for one year. If the student were discovered by private examination to be unfitted after only one year's study to proceed to the public examination, he was required to take one or more of the courses a second time. Finally, in order to assure a practice knowledge of pharmacy, every student must have served an apprenticeship to some reputable physician. Upon meeting these requirements and passing a private examination by the medical professors and trustees, the student was permitted to appear for his public examination.

As for the doctor's degree, this was conferred on those, who, having taken the bachelor's, practiced three years, were 21 years of age or more, and submitted and defended a thesis on a medical subject. When the first students qualified under this regulation in 1771, the trustees directed that their examination be private and that it consist of "a few Questions in Latin" on the subject of their theses.[16] Thus both in the bachelor's and doctor's degree the Philadelphia requirements recognized to a greater degree than Edinburgh's seemed to do, the importance of practical experience as a foundation and qualification for a degree.

In the spring of 1768 ten students were found to have met the requirements for the bachelor's degree at the College of Philadelphia, and were graduated. Hailed as "the Birth-day of medical Honours in America," this happy occasion attracted a good deal of attention, for it marked another coming of age of colonial society.[17] Of this first examination apparently no record survives. But of the examination of 1769 we have an almost unique document—a list of all the questions asked in the public examination of that year, complete with the names of the professors who asked the questions and the candidates of whom they were asked. Eight young men were judged ready for graduation in this year. Their names were James Armstrong, Josias Carvil Hall, John Hodge, John Houston, Thomas Pratt, Alexander Skinner, Myndert Veeder, and John Winder. Their public examination was held on May 30.

THOMAS PARKE'S NOTES

In the audience that day, with a small notebook on his knee and an inkhorn hanging from the nearest chair, an ambitious young Quaker

[14] Frederick C. Waite, "The Degree of Bachelor of Medicine in the American Colonies and the United States," *Yale Journal of Biology and Medicine*, X (1937–8), 309–333.

[15] Joseph Carson, *History of the Medical Department of the University of Pennsylvania* (Philadelphia, 1869), 59–61.

[16] *Ibid.*, 216; Thomas H. Montgomery, *A History of the University of Pennsylvania from its Foundation to A.D. 1770* (Philadelphia, 1900), 483–485.

[17] Carson, *op. cit.*, 69.

intently copied down every question the professors asked. Thomas Parke was Cadwalader Evans' apprentice; he had come up from Chester County three years before, was now attending the medical lectures, and may already have been dreaming that one day he would follow his masters to Britain and study at London and Edinburgh. But his immediate purpose as he plied his pen this day was to get a record of all the questions the professors might ask him when he came up for his degree in the same place the next year.[18]

Parke's notes of the 1769 examination are a concrete reflection of the medical curriculum at Philadelphia at that time. They are one of the few things of the kind that have survived. The questions show several things. In the first place, most of them could be answered simply, by a word, a number or a definition. They were in effect only the professors' didactic lectures turned into interrogatories. In the public examination, unlike the private, no experiments were cited, no problems posed, no hypothetical questions asked. The examination was a better test of memory than of reasoning and understanding. In the second place, although the public examination was essentially an exhibition, the trustees of the College and possibly the public as well had the right to question any candidate, and they sometimes did. Finally, these questions were similar in character to those asked at other American medical colleges at this time.[19]

Thomas Parke made his notes on the last leaves of a notebook he filled two years before with extracts from Macquer's *Elements of the Theory and Practice of Chemistry*. Catalogued under "Of the Principles of Bodies," which is the subject of the material taken from Macquer, the notebook is in the library of the College of Physicians of Philadelphia. Each of the questions Parke copied has been expanded in the following transcript from the abbreviated form in which it was recorded; and spelling and capitalization have been modernized. Thus, for example, Parke's note, "Wt. Analytic & Synthetic" appears here as "What is analytic chemistry; what is synthetic?" In some cases Parke recorded the name of the student being examined; in a few cases he inserted an answer. Where no student name was given, the paragraphing is conjectural.

SHIPPEN'S QUESTIONS

Dr. William Shippen, Jr., professor of anatomy, opened the examination with questions on his subject.[20]

What is anatomy, &c? What is a skeleton? How is it divided, &c? What is contained in the skull? Where do the nerves arise? How many bones are there in the head? What bones constitute the trunk? What is the shape of the spine? What is the shape of the vertebrae?

What is contained in the thorax? How are the lungs covered? What sort of a membrane is the pleura; and how many membranes are there? How is the heart covered? What is the use of the lungs, &c? Does all the blood in the body go through the lungs? What is the name of those vessels that go through the lungs? What is the use of the lacteals and nerves? What divides the two cavities of the body? What is the shape of the diaphragm and its substances? How does its shape change? What communication is there between the thorax and abdomen. How many perforations

[18] On Thomas Parke see Whitfield J. Bell, Jr., "Thomas Parke, M.B., Physician and Friend," *William and Mary Quarterly*, 3rd ser., V (1949), 569–595, and "Thomas Parke's Student Life in England and Scotland, 1771–1773," *Pennsylvania Magazine of History and Biography*, LXXV (1951), 237–259.

[19] Reginald Fitz, "The Surprising Career of Peter La Terrière, Bachelor in Medicine: Being an Account of the Life and Adventures of a Harvard Medical Student who Received his Diploma in 1789," *Annals of Medical History*, 3rd ser., III (1941), 265–282, 395–417, contains a colorful account of the medical education and graduation of one student. Extracts from La Terrière's journal are translated and printed in *Boston Medical and Surgical Journal*, CLXII (1910), 517–524.

[20] Corner, *op. cit.*; also *D.A.B.* See an unknown student's "Lecture Notes on Anatomy" in College of Physicians of Philadelphia Library, and other notes of Shippen's lectures, by William McWilliams, 1777, in the same place, and by an unknown student, 1786, in University Archives, University of Pennsylvania.

are there through the diaphragm. *Answer:* three.

Pratt: How is the abdomen divided? What are these distinctions? Why are there not such in the thorax? Where is the liver situated? Where are the spleen, and stomach, and kidney? What is the use of the liver? What is the bile secreted from? What is the *vena porta?* What is the *vena porta* made of? What is the use of the venal blood's being taken to the liver?

Hall: How is the bile secreted? What are the secretory vessels? What do the arteries terminate in, in the liver? What does the *porus bilis* terminate in? Does the bile regurgitate? How is the bile propelled into the duodenum?

What is the shape of the stomach? How does the aliment pass on account of the valve there? How many coats has it? *Answer:* three. Is the muscular coat of the stomach strong enough to perform digestion? How is it performed? Where is the aliment propelled to from the stomach, and how? What is the pylorus? What is the difference between the duodenum and the rest? Why is the gut tied down?

Where does the pancreatic juice come from? What is the use of the bile? Where are the lacteals situated? By what power do these lacteals take up their fluid? Where do they carry it to? Where is the thoracic duct? What is its use? Where does it carry its fluid? Does the action of the thoracic duct depend on the heart? How is its fluid propelled? What is the bile mixed with?

How is the blood carried to the different parts of the body? What is an artery, &c? Is there any peristaltic motion in the arteries? *Answer:* yes. What do the arteries terminate in? What is the use of veins? What is the difference between arteries and veins? Have all veins valves? Why in the veins of the extremities are there as many veins as arteries [sic]? What are lymphatics? How do you prove them absorbent? What is the urine? Where is it secreted? *Answer:* kidney. How is it carried from the kidney? Where do they carry it to? Can the urine regurgitate?

What are the contents of the pelvis? *Answer:* nothing between bladder and rectum. How many pairs of muscles are there on the abdomen? How are the viscera covered? What is the peritoneum? Is it moist or dry? What is there particular in the first great gut? Whence rises the gravel?

At this point the Rev. Mr. Richard Peters, formerly Secretary of the Province, now rector of Christ Church and St. Peter's, an active trustee of the College, interrupted to ask the student, "Are stones ever generated in any other part of the body than the bladder?" His question was not an idle one. Three years before he suffered from "a severe Fitt of the Stone," which his physician, Dr. Morgan, estimated was "as large as a pigeons Egg at least." Throughout his illness Mr. Peters had sought all the information he could get on his condition.[21]

Such interruptions as Peters' were an expected part of these public examinations, but they were not the less upsetting for all that. On such an occasion at Harvard in 1789 a student was asked by a physician in the audience what a sudorific is and which is the most efficacious one. "A sudorific," the student replied in a definition that was often repeated, "is anything that induces perspiration; and the best sudorific is to appear before such a large and honorable company as this, to answer their questions scientifically and properly."[22]

Shippen had only two more questions:

Where does the artery end and the vein begin? How is it known?

MORGAN'S QUESTIONS

Now Dr. John Morgan, professor of theory and practice, began to examine the candidates on chemistry. He had taught the subject since 1765, but would soon confine himself

[21] Richard Hockley to Thomas Penn, July 4, 1766, Penn Mss., Official Correspondence, X, 45, Historical Society of Pennsylvania; Hubertis M. Cummings, *Richard Peters, Provincial Secretary and Cleric, 1704–1776* (Philadelphia, 1944), 286–288.

[22] David Heald, "The Harvard Medical School in 1788–89," *Boston Medical and Surgical Journal*, CLXII (1910), 522.

to his proper subject, for Benjamin Rush was expected soon to return from abroad to occupy the chair of chemistry which Morgan had held open for him.[23]

Armstrong: What is chemistry? How are they distinguished? What is analytic chemistry; what is synthetic? What are bodies? How many kinds of elements are there? What is an atom? What are chemical principles? What are mixts? What is a compound? What are their differences? What is a decompound; what is a super-decompound?

How are sensible bodies resolved? How are aggregates divided? How do constituting and integrant parts differ? What is nitre and how is it divided? How is acid separated and how is it promoted? How is alkali obtained? *Answer:* by adding inflammables. What is vitriolic acid? Is it native? What is it combined with? What is the composition of sulphur? Is it ever found united with earthy substances? What is the effect when it is applied to any other acid, or alkali, or water?

How do you dissolve iron in vitriolic acid? *Answer:* dilute. What is the phenomenon here? What is phlogiston? What is the specific gravity of vitriolic acid? What are the names it is distinguished by in the books of chemistry? Are they all different acids? How does not the acid of sulphur differ from the acid of vitriol? From what substances is acid of vitriol chiefly obtained? *Answer:* sulphur.

How many classes of bodies are there in chemistry? What is a saline body? How many kinds of salts are there? Why are they called simples? How many kinds of acids are there? *Answer:* four. Why are they called by these names? *Answer:* from the substances they are obtained from. How many kinds of compound salts are there? What are the marks of an acid? What is that of an alkali? Is there any other mark of an alkali than that of turning syrup of violet green? What are the effects of uniting an acid and alkali together? Can they be united unequally?

Skinner: How many kinds of compound salts are there? What are metallic salts? Where is there an instance of this salt? What are earthy salts? What are purging salts? What is the effect of an acid united with an earth? What is effervescence? What is the effect of adding an alkali to an earthy salt? How many kinds of alkali are there? What is a fixt alkali? What is a volatile alkali? Do these differ from one another? Do the volatile alkalis, when united with alkali, form the same kind of salt as the fixt? How many kinds of ammonia are there? How many neutral salts are there? What is vitriolated tartar? What are Glauber's salts? What is the difference between cubic and common nitre? How is nitre obtained? How many kinds of salt does muriatic acid afford? What is digestive salt? What is common salt? What are spirits mindereri? What salt is Glauber's salts obtained from? What is an inflammable substance? What is the distinction between an inflammable and ignited body? How many kinds of inflammable bodies are there? How many kinds of oils are there? What kinds are they?

Pratt: Why are they called by these names? How many kinds of vegetable oils are there? What is expressed, essential, and empyreumatic oil? In what quality does an expressed oil differ from essential oils? What is the quality of empyreumatic oil?

Winder: How many kinds of earthy bodies are there? What is an absorbent earth? What is a crystalline earth? What is an argillaceous body? What kind of earth is a calcareous one? Give an example. *Answer:* quick lime. What is the particular quality [of quick lime]? What is fixed air? Is there any surrounding us in the atmosphere?

What is the use of crystalline earth? *Answer:* to make glass. Is the action of fire alone sufficient to convert it into glass? What is quick lime? What do the changes in the qualities of bodies depend upon? What is necessary? What is attraction; what is elective attraction? Give an instance. How is elective

[23] William S. Middleton, "John Morgan, Father of American Medical Education," *Annals of Medical History*, IX (1927), 13–26; also *D.A.B.* John Hodge's notes of Morgan's course in chemistry, 1766, are in the College of Physicians of Philadelphia Library; they were studied by J. S. Hepburn in "Smith and Morgan, Our First Chemists," *General Magazine and Historical Chronicle*, XXXV (1933), 491–510.

attraction accomplished? *Answer:* in single and double. What is single and double elective attraction? How may kinds of distillation are there?

KUHN'S QUESTIONS

This completed Morgan's questioning. But Mr. Peters arose again and "questioned Armstrong concerning acids and alkali & the first motion of bodies." The third member of the medical faculty, Dr. Adam Kuhn, professor of materia medica and botany, now concluded the examination of candidates.[24]

Armstrong: What is the definition of materia medica? How are astringents known? Do they act on the simple or moving solid? How are astringents divided? When are vegetable astringents ordered as well as fossils or minerals? How do calcareous astringents act?

Hodge: What calcareous substances are used as astringents? Will any of these substances act in their native state, as iron? How are chalybeate waters known? Is water ever impregnated with copper? How is this known? Is there any difference in the effects of copper and iron? *Answer:* yes. Is lead a safe medicine? *Answer:* no.

Houston: What parts of the body do emollients act on? Which are the principal ones? Do they differ in their effects? Is cold water an emollient? What is the advantage of using warm water? What parts do stimulants act on? When are they indicated?

Skinner: What are the effects of stimulants? Is there any disadvantage in a long use of stimulants? What is Peruvian bark? Is it indicated in every fever? *Answer:* no. What fever is it ordered in? What is the best method of giving the bark? *Answer:* in powder.

Veeder: What are sedatives? On what parts do they act? What are the principal ones? What are the effects of opium? Is opium useful in all pain? *Answer:* no. Is it useful in all spasmodic complaints? Is it of service in hemorrhages? *Answer:* yes, in some.

Pratt: What are the effects of cold baths?[25] *Answer:* astringent. In what diseases and cases is it proper? What is the effect of it, &c? Why is the cold felt sensibly as well as the heat? Is the cold bath useful in consumption and other weaknesses. *Answer:* no. How is epilepsy cured? Is it good in hysterics? *Answer:* yes. In hypochondria?

Winder: What are emetics? What is their effect? Is there any difference in emetics? What is a sialogogue? Which is the principal one? *Answer:* ☿ (mercury). Will mercury have any effect on the body in the crude state? What is the best form for exhibitions? Is a salivation always necessary for curing the lues venerea? Will ☿ have its proper effect without salivation? Then which is the proper method of giving it? What are the advantages of giving the milder preparation of mercury?

Hall: What are the effects of blisters? Are they stimulating? Why are they used in topical inflammations? What are the effects of cantharides when taken internally? What are purges? Which are the mildest? What are aloetic purges? What is the dose of aloes? How are the purgative virtues of rhubarb increased? *Answer:* by calomel.

All the young men acquitted themselves honorably, even the two whom Mr. Peters quizzed so unexpectedly; and on June 30 they received their degrees. Four of the eight had places on the commencement program. Hall delivered an oration in honor of medicine and Winder recited another on the most probable method of reaching a good old age; while Skinner and Hodge debated "whether Medi-

[24] Marion E. Brown, "Adam Kuhn: Eighteenth Century Physician and Teacher," *Journal of the History of Medicine and Allied Sciences*, V (1950), 163–177; also *D.A.B.* Parke's notes of Kuhn's lectures on materia medica are in the library of the Pennsylvania Hospital; another set, by an unknown student, are in the College of Physicians of Philadelphia Library; and facsimiles of John Archer's notes of Kuhn's lectures, 1768, are in the library of the School of Medicine, University of Pennsylvania, and the Medical and Chirurgical Faculty of Maryland, Baltimore.

[25] Kuhn's Edinburgh dissertation was *De lavatione frigida*; he customarily devoted considerable attention to the subject in his course.

cine hath done most Good or Harm in the World."

In the Composition of these Exercises, the young Gentlemen gave full Proofs of Learning, as well as of a thorough Acquaintance with their Subjects, and the History of Physic, and they were honored with the close Attention, and warm Approbation, of the Audience. Mr. Skinner's Part of the Forensic Dispute in particular, seemed to afford singular Entertainment, from the candid Freedom which he took with his own Profession, and the very humorous Manner, in which he attempted to prove that Medicine had done more Harm than Good in the World; which Position of his was, however, very seriously and fully replied to by Mr. Hodge.

Provost Smith then delivered a charge to the graduates in arts and Dr. Thomas Bond, a trustee of the College, whose clinical lectures at the Pennsylvania Hospital were required of all candidates for a degree, addressed the new physicians "in a Manner so truly *feeling* and *affectionate* that it could not fail to make a serious Impression on those for whom it was designed."[26]

The regulations of 1767 remained in force at the College of Philadelphia until the institution was dissolved by an act of Assembly during the Revolution. Under them ten men were graduated in 1768, eight in 1769, one in 1770, seven in 1771, and two in 1773. Though the war interrupted medical instruction, it did not suspend it entirely. Students continued to come to the city, the Army sent surgeon's mates there to be instructed in their business, and the new University of the State of Pennsylvania offered courses, gave examinations, and granted degrees. With the reestablishment of the College in 1789, the medical faculty was reorganized and new regulations for the granting of degrees were adopted.[27] The most important change was that the degree of bachelor of medicine was dropped. The expectation that bachelors of medicine would prepare a thesis and take an examination for the doctorate had proved a vain one: of 29 persons graduated between 1768 and 1774 only 6 qualified for the higher degree. And it was significant of the level of American education and the spirit of cultural nationalism that the thesis might be written either in Latin or in what Dr. Benjamin Rush called "the language of the United States." The new regulations brought the College still closer to the Edinburgh practice, but, to a greater degree than the Scots, the Americans recognized the importance of practical work.

Specifically the requirements for the doctor's degree were two years of study at the College and three years of apprenticeship to "some respectable practitioner"—only two years were required if the candidate lived in the country. The candidate must be at least 21 years of age. As for examinations, the candidate's fitness to take the degree was determined by private examination; he must then write the answer to a medical question and the diagnosis and treatment of a medical case, and defend both before the faculty; next he must submit to a public examination "before the Trustees, the Provost, Vice Provost, Professors and Students of the College;" and finally he must write a thesis, have it approved by the professors and printed, and defend it "from such objections as may be made to it by the Medical Professors" at the Commencement.

There is ample evidence that this final examination on the thesis might be anything but a formality. Pierre La Terrière at Harvard in 1789 was questioned by some members of the audience, answered correctly, and then proceeded confidently to question *them*.[28] But the final examination of Charles Caldwell at Philadelphia in 1796 exceeded all limits of restraint; the conflict between student and examiner, Caldwell remembered, was "cutting and severe." The facts were these:

When he was on service with the militia in western Pennsylvania during the Whiskey Insurrection, Caldwell, then a student of medicine, learned that cold water is sometimes helpful in the treatment of fevers, and

[26] *Pennsylvania Gazette*, July 6, 1769; Carson, *op. cit.*, 214–215.

[27] *Ibid.*, 95.

[28] Heald, *loc. cit.*, 522.

he communicated this discovery to his Philadelphia teacher Benjamin Rush. Rush presented the idea in his next course of lectures, but without crediting Caldwell with the discovery. A few weeks later, now returned to Philadelphia as a student, Caldwell had the opportunity to present his theory in a paper to the Philadelphia Medical Society; this he did with a complete statement of Rush's treatment of him in the matter. Dr. Rush was not present at this meeting, but some of his partisans in the audience joined the issue, attacking Caldwell, and carried a report to Rush.

A few months later Caldwell presented himself for final examination on his thesis. In the original draft, which dealt with three common diseases of children, he had included a brief account of his earlier clash with Rush, but on the advice of the dean of the faculty of medicine had excised this as irrelevant and improper. Nonetheless, when Dr. Rush began to question Caldwell on the thesis, he chose to discuss the expunged passage. Caldwell insisted that he should be examined only on the thesis as printed. The Provost, who was presiding at the examination, upheld him. But Rush was insistent, replied by waving a copy of the thesis in which he said the offensive passage appeared. Stepping quickly to Rush's side, Caldwell snatched the pamphlet from his hand, looked quickly at it, pronounced it a spurious copy, and charged Rush with knowing that it was spurious. The exchange between the two men mounted in passion until Rush, at a peak of exasperation, cried out, "Sir, do you know either who *I* am, or who *you* are yourself, when you presume thus arrogantly to address me?"

"Know you, sir!" Caldwell replied, as he remembered, calmly but contemptuously; "oh, no; that is impossible. But as respects myself," he continued in a retort that became part of the tradition of Philadelphia's medical schools, "I was, this morning, Charles Caldwell; but, indignant, as I now am, at *your* injustice, call me, if you please, *Julius Caesar, or one of his descendants*!"

A moment of awful silence followed, until the Provost quickly rose and directed the exercises to continue. When the time came for the professors to sign the graduates' diplomas, Rush refused to affix his signature to Caldwell's. Caldwell, however, had the last word. He appealed to the audience to decide whether he had not been more insulted than insulting, and publicly informed Dr. Rush that he would soon show the professor of the institutes of medicine that he did not need his signature of approval.[29]

Public commencements today are more seemly affairs. How they came to be so is, no doubt, another story.

[29] Charles Caldwell, *Autobiography* (Philadelphia, 1855), 232–236, 239–246.

Memoir of James Harold Austin (1883–1952)*

By O. H. PERRY PEPPER

EVERY step in the life of James Harold Austin testifies to the high quality of his character and ability. He possessed the rare combination of a keen incisive brain with a sympathetic willingness to sacrifice his own work and time to help others. Also he combined deep religious convictions with an equally profound love of science.

Born in Philadelphia on September 22, 1883 Harold Austin graduated from the Episcopal Academy in 1902, the College and the Medical School of the University of Pennsylvania in 1905 and 1908. In each of these stages his brilliance was evident. He led his medical class and was elected to all three honor societies: Phi Beta Kappa, Sigma Xi and Alpha Omega Alpha. After an internship at the University of Pennsylvania he became an instructor in pathology in the same school and began to display his life-long interest in research. Next he accepted a part-time clinical position, but pathology and biochemistry were always closer to his heart.

In 1917 he entered the military service and was bitterly disappointed that his scientific qualifications kept him in this country. In this instance the army was wise, as the record of his work shows; he led the pneumonia work at Camp Upton, gave courses in the Dakin procedures for example, and that his services were appreciated is proved by his rising to the rank of Major.

After the war he served as Chief Resident at the Rockefeller Hospital for three years and was also an Associate in the Rockefeller Institute. In 1922 he returned to his Alma Mater to be Professor of Research Medicine and Director of the John H. Musser Department of Research Medicine, positions he held for about 20 years.

Active at all times, he published some 80 papers; for 10 years was Editor in Chief of the *Journal of Clinical Investigation* and was an associate editor of *Medicine*. He was an active member of all of the leading societies in the fields of pathology and medicine, but he was especially active in the College of Physicians of Philadelphia, editing the *Transactions* from 1933 to 1936 and holding the elective office of Secretary from 1937 to 1946. With characteristic self effacement he stepped aside from higher honors. In addition Dr. Austin served on the American Board of Pathology, and for several years after World War II was Chairman of the Philadelphia County Medical Society Committee on Civil Defense. To this duty he gave much time and energy.

In 1942 he became Director of the William Pepper Laboratory of Clinical Medicine of the Hospital of the University of Pennsylvania and held this post until he reached the age of retirement. In this position he accomplished great improvements in the laboratory work of the Hospital and especially in its blood bank. Always he was available to others to give them from his wide knowledge of chemistry, physics and mathematics, assistance in their research problems or in the preparation of their statistical data in which field of medicine he was one of the first to become expert. He had an amazing ability to go at once to the root of a complex problem, and his advice was often sought and always freely given.

No sooner relieved of one task than he assumed another and in 1949 he became the first Executive Secretary of this College. In this newly established position which he held

* Written and published at the request of the Council of the College of Physicians of Philadelphia. Read before the College, 4 March 1953.

until his death, he developed a pension system for the employees, improved the Life Fellowship program and helped organize the campaign for a new building fund. As part of this campaign a separate fund named after Dr. Austin is being raised for the Library in grateful memory of him. His activities as Executive Secretary demonstrated how much this College needed an enthusiastic, capable man in this position.

At this point I beg your indulgence to reminisce briefly about my long friendship with Harold Austin. We were classmates in college and medical school and soon became close friends. We studied together, tried to learn German; played chess and visited in each other's homes. In medical school we both joined one of the extracurricular quiz groups so popular in those days. After interning together we belonged to a small journal club with Outerbridge, Krumbhaar, Laws, Willard and a few others.

In 1911 Alfred Stengel offered us the opportunity to undertake what was then a novelty, an almost full time academic program. We served in the wards in the mornings, and in the afternoons worked with Dr. Richard M. Pearce in research in the haphazard manner of those days. I look back with embarrassment at our brashness in venturing into such fields as chemistry, pathology and hematology—in none of which were we adequately trained. We published together seven papers, one of which was quoted in Otto Folin's authoritative text book.

Very soon it became clear that Harold was more keen on the laboratory and I on the clinic; our activities separated but our affection never lessened. We joined the same intercity visiting medical club; we served together as officers of this College.

This intimacy of fifty years qualifies me to testify that Harold was a man of exceptional ability, honesty and modesty.

Harold Austin is survived by his wife, who was Thelma F. Wood, and by three children. Those who visited their home were always impressed by the atmosphere of religious faith, and by an interest and awareness of all things intellectual. The former is certified to by Dr. Austin's membership on the Board of Vestry of Holy Trinity Church in Philadelphia; the latter by his wide reading and many fields of knowledge.

Another side of Harold Austin, complementing the others, was his love of the outdoors; if he had not been a doctor and medical scientist he might well have been a naturalist. Ornithology was perhaps his favorite branch in this field. He was fond of walking in the country, alert all the time for any bird in tree or shrub. His sudden death on March 29th, 1952, while taking such a walk is one many might well envy.

By his death this College lost a devoted Fellow and a valuable servant. Those of us who knew him lost a true friend.

Memoir of George Woodward (1863–1952)*

By WILLIAM U. McCLENAHAN

WHEN Dr. George Woodward died at the age of 88 on May 26, 1952 at his home in Chestnut Hill few members of this College knew him personally. At the time of his death he was the third oldest member of this College. His claim for fame in medicine was negligible. Few physicians, however, outside their profession have done more for their community, their city, and their state. His time was devoted and dedicated to human welfare and certainly this is the essence of medicine at its best.

It is quite proper, too, that a man who wrote his brief autobiography entitled "The Memoirs of a Mediocre Man" should have his memoirs read tonight by a mediocre man, a medical colleague, a neighbor, one of his former tenants, and a person who after years of association with his patient feels that he had received far more than he had given.

I shall never forget the first call I ever made to Dr. Woodward. A perfect spring afternoon, the winding beautiful approach to Krisheim, the Woodward home. A young physician hurrying to answer the call, spirits dragging and self-confidence shaken with the realization that he had to treat a doctor, an elderly person quite naturally fixed in his ways and notoriously a hard individual to handle as rumor went. With knees shaking and palms moist, in a large living room before a huge fire-place I waited. Suddenly the doctor appeared. A tall, slender, active figure in gray tweeds and knickerbockers, open shirt and no tie. His quiet voice, his deep-set blue eyes, sometimes piercing, often twinkling with mirth, and a smile completely disarming. I realized instantly that I was dealing with a nonconformist, a completely uninhibited and fearless individual. His mind was keen and inquisitive, youthful in its flexibility and breadth of interest. We sparred for a few minutes both intent upon sizing up each other. I led with the request for a thermometer and he countered by disappearing on the run and returning with a thermometer in his mouth. Some subconscious reflex, possibly my guardian angel, made me request that I inspect the thermometer which he surrendered grudgingly. The thermometer registered 107 and, upon questioning, the doctor admitted it may have been washed in warm water. Whether this was intentional or accidental I shall never know. I have my own opinion. At any rate figuratively speaking we touched gloves and ever after enjoyed the varied tussles every physician encounters in his geriatric practice.

George Woodward, the fifth generation to live on the same land was born on June 22, 1863 in Wilkes-Barre, Pa., the son of Stanley and Sarah Woodward. His father was a successful lawyer and an ardent Democrat. His grandfather was the Chief Justice of the State of Pennsylvania. For four generations the eldest son was a Judge Woodward.

Two persons influenced him the most in his early life. His maternal grandmother, a staunch New Englander and a Presbyterian Sunday school teacher for 50 years had a brilliant mind and, contrary to custom among women of those days, was keenly interested in politics and public affairs. She was a stern disciplinarian and all through college wrote him weekly letters which he describes as "delightful letters written on scraps of paper of any color or size or shape." The person chiefly responsible for his interest in medicine was his family physician. Dr. Woodward has described him as follows: "Our family physician was a splendid example of the general practitioner. He healed and comforted and we all worshipped him. Indeed, he is one of the unsung heroes of the world.

* Written and published at the request of the Council of the College of Physicians of Philadelphia. Read before the College, 4 March 1953.

To have such power, therefore, decided me to study medicine. I was in Yale College at the time somewhere near the bottom of my class."

At Yale from which he graduated in the Class of 1887 his chief extra curricular activities were the Glee Club in which he was an active member for four years and his Senior Society, Skull and Bones.

He graduated from the University of Pennsylvania Medical School in 1891. His three friends and classmates later to become famous in medicine were Drs. Joseph Sailer, John C. Clark, and Joseph Bloodgood. Fortunate indeed, he was to have as professors, and he frequently referred with pride to this fact, William Pepper, Sr., William Osler, Joseph Leidy, and Horatio Wood. His marks in his senior year suffered from the ever present problem of a medical student's education,—courtship and frequent walks along the Wissahickon with a most attractive Chestnut Hill debutante.

Luck and keen foresight favored the young doctor's acceptance for internship in the Lankenau Hospital. The Board was captivated by his German in a conversation composed by a German friend and memorized by the applicant two hours before the meeting. A casual reference to a recent trip to Munich and the beer in the Hofbrauhaus elicited an uproar of ah's, oh's, wunderschöns, and ach lieber Gotts. The managers forgot his examination, and the rest of it was perfunctory. Secondly, during his third year in medical school he had deliberately cut all attendance at the eye clinics. The ophthalmologist of the hospital was taken ill the day of his examination and no questions were asked on this subject. Two physicians made an outstanding impression in this period of his career, Drs. J. William White and John B. Deaver.

After a year's practice in New Haven, Conn., he became engaged to Miss Gertrude Houston of Chestnut Hill. Her parents imposed two conditions: (1) He must never give his wife allopathic medicine. (2) He must live in Philadelphia.

He did not hesitate a minute. On October 9, 1894 he married Miss Houston. A three weeks' honeymoon was spent touring Eastern Pennsylvania and Western New York, transportation being provided by a borrowed buggy and a horse named Adam.

Dr. and Mrs. Woodward had five children.

Henry Howard Houston Woodward was the eldest. At his birth Dr. Woodward officiated, ably assisted by the Scotch cook, Janet Henderson. Houston Woodward, a member of the Lafayette Escadrille was shot down and killed at Montdidier in 1918. (2) George Woodward, Jr., the present director of the Woodward Estates. (3) Stanley Woodward who inherited his father's interest in politics, became a career diplomat in the State Department, and served with distinction as our recent ambassador to Canada. Just how a son of George Woodward became the Chief of Protocol in a Democratic administration is a question only God can answer. (4) Charles Woodward, a lawyer, active in all civic affairs. (5) Gertrude, better known as Quita, the youngest child, was the only daughter. She was the darling of her family, loved and admired by a host of friends. Her untimely death at the age of 24 from Hodgkin's disease was the great sorrow of the doctor's life, leaving a lasting impression on his heart, a mellowness of spirit, and a profound understanding of others' suffering.

His first medical assignment in Philadelphia was to the staff of the Pepper Laboratory where he became interested in the study of milk. He became an early director of the Walker Gordon Milk Co., and was responsible for many improvements in the milk industry. Through the influence of Dr. Charles H. Frazier he was recommended to the Mayor of Philadelphia as a member of the Board of Health and that opened the door to politics. Before drawing the curtain upon what he describes as a mediocre medical career one incident deserves mention. Typhoid fever was

rampant in Philadelphia at this time. To stimulate public interest he studied the city's water supply. Every sewer and privy discharging into the Schuylkill River from Philadelphia to Reading was photographed and samples of every source of pollution were taken and analyzed. After his report was made the city government had to spend the money for slow sand filters and typhoid fever practically disappeared. In spite of this Mayor Samuel Ashbridge, obviously annoyed by the public reaction, was very angry with the Board of Health and had it abolished at the next Legislature. He said that it had fouled its own nest. A most curious statement indeed.

In 1895, persuaded by Sister Ruth, a deaconess of the church, he undertook the real estate business, building first semi-detached houses for the poor. Today the Woodward Estate is one of the largest in the city and has done a remarkable job in civic improvement and the provision of attractive homes at minimal cost.

Dr. Woodward entered Pennsylvania politics in 1918 when he was elected to the State Senate where he served continuously with distinction until 1947. He was elected to his last two terms of office without a campaign. I should like to quote the newspaper report of his initiation into the Senate.

"Dr. Woodward's arrival in Harrisburg created probably the greatest sensation since the threatened invasion of the Southern army of Robert E. Lee. Nonchalant, pleasant, and utterly unselfconscious, Dr. Woodward entered the chamber wearing gray golfing knickers and smoking a pipe. He approached the two-barred brass railing that enclosed the senatorial desks and eyed it casually, a tall, spare figure with a catlike tread and the lines of a pole-vaulter. Hardly pausing in his stride the senator vaulted over the brass railing to the accompaniment of shocked gasps from his colleagues and a ripple of decorous applause from the gallery. Then he walked to his seat, dropped into his chair and threw a long, stockinged leg over a chair arm. . . . It was the beginning of a distinguished career." Soon he was publishing a little blue-covered pamphlet called "Pennsylvania Legislator" in which he reported the proceedings of the Senate to his constituents. Not only as a legislator but as a writer he demonstrated unusual ability.

As an associate of Thomas Raeburn White of the Committee of 70 in 1919 Senator Woodward became a leader of the legislative group named to draw up the new City Charter Act. The two chief factors in this measure to clean city government were a civil service code for city workers and restrictions on political activity. This reform not only eventually fathered the present City Charter in Philadelphia but had far reaching effects on other states. The City Manager system of municipal government was started in Cincinnati, Ohio in 1925. The good he did which is known publicly is nothing compared to benefactions in many other fields—individual, church, and educational in character. He was not a man to publicize his good works. In listening to previous memoirs of our past distinguished colleagues, I have often wondered whether we have not too frequently omitted to mention the Doctor's wife, the person who quietly, without recognition and reward has contributed much to her husband's success. Certainly in Dr. Woodward's case this is true. He would be the first to recognize this fact. In closing I should like to quote a passage from his book, "The Memoirs of a Mediocre Man." The language describes Dr. Woodward's simplicity, directness, humility, and priceless sense of humor.

"I am sure I chose the wrong profession but I must say the study of medicine fascinated me. I gave up my Christmas holidays to study anatomy and microscopic slides (histology, to be exact). I must have won high marks in my first two years but not in my third. The course was then only three years. This made the third year almost an intense agony of effort. It was too much for me. The examina-

tions were oral. I know I blundered in therapeutics and obstetrics and the practice of medicine. In this last I had Dr. William Pepper and he asked me to tell him all I knew about measles. If he had asked for elephantiasis or lead poisoning or bubonic plague, I could have told him all about it, but a simple little thing like measles; it was too little. In another examination I had the bad luck to be asked about two lectures from which I had played hooky to take a country walk with a Chestnut Hill girl. As the same girl finally agreed to marry me and without whom I would never have accomplished anything in life, I do not regret my failure to answer these two questions."

List of Contributors to the Building, Development, and Austin Funds, and to the Library of the College*

Note: In the College's current campaign for funds, contributions from its Fellows go into the *Building Fund;* contributions from non-Fellow friends of the College go into the *Development Fund;* the *James Harold Austin Memorial Fund* consists of contributions made specifically in memory of Dr. Austin; the *Contributors to the Library* here listed are industrial organizations which have made donations specifically in support of the library.

Building Fund

Addison, William H. F.
Adelizzi, Richard I.
**Adler, Francis Heed
Aegerter, Ernest E.
Aiken, Thomas G.
Alexander, Fay Knight
Allbritten, Frank F.
Allen, Frederick H.
Alpers, Bernard J.
†Anspach, Brooke M.
Appel, Kenneth E.
Appelman, Leighton Francis
Aronson, Joseph D.
Aronson, Roland S.
Astley, G. Mason
**Atlee, John L., Jr.
Atlee, William A.
†Austin, J. Harold

Bach, Theodore F.
Bacon, Emily P.
Barden, Robert P.
Barnshaw, Harold D.
Bartle, Harvey, Jr.
Bates, William
Bauer, John T.
Baumann, Frieda
†Bazett, Henry C.
Beardsley, E. J. G.
Beecham, Clayton T.
Beerman, Herman
Behrend, Albert
Behrend, Bernard
Behrend, Moses
Beizer, Lawrence H.
Belk, William Parks
Bell, Benjamin Tertius
Biddle, Sydney Geoffrey
Bixby, Edward W.
Blady, John V.
Block, Frank B.
Blumstein, George I.
Bockus, Henry L.
Boles, Russell S.
Bonney, Charles W.
Bortz, Edward Le Roy
Borzell, Francis Frank
Bostwick, Delazon Swift
Bothe, Frederick A.
Boucot, Katharine R.
Bourland, Henry
Bradley, William Nathaniel
Briscoe, Clarence Conway
Bromer, Ralph S.
Brown, Charles L.
Brown, Claude P.
**Brown, Henry P., Jr.
Brown, Robert B.
Burnett, W. Emory
Burros, Harry M.

Cadwalader, Williams B.
Camero, Anthony R.
Campbell, Edward H.
Cantarow, Abraham
Carey, Lawrence S.
Carpenter, Chapin
Carson, John B.
Castallo, Mario A.
Caswell, H. Taylor

* As of 14 March 1953. The list includes donors named in earlier lists published in the *Transactions & Studies*, February, 1951, and April, 1952.
** Contributor of $1,000 or more.
† Deceased.

**Chamberlin, George W.,
Chapman, John P.
Chouké, Kehar S.
Ciccone, Emmett F.
Clark, John K.
Clarke, Francis Mann
Classen, Charles H.
Clerf, Louis H.
Cloud, J. Howard
Cohen, J. Gershon
Cohen, Leon Solis
Cohen, Louis B.
Colonna, Paul C.
Conger, Kyril B.
**Cooper, David A.
Cornelius, Chalmers E.
Cornell, Walter S.
Corson, Edward F.
Cowan, Alfred
Craig, Frank A.
Crane, A. Reynolds
Creskoff, Adolph J.
Cross, Sumner H.
Crump, Jean
Custer, R. Philip
Cuttle, Tracey D.

Dannenberg, Arthur M.
Davis, David M.
Davis, Perk Lee
Deaver, J. Montgomery
Dehne, Theodore L.
De Long, Perce
De Palma, Anthony F.
Dewees, A. Lovett
Dillon, Edward S.
Dintenfass, Henry
Dohan, Francis Curtis
†Dorrance, George M.
Dripps, Robert D.
Dublin, George J.
Dugger, John H.
Duncan, Garfield G.
Durant, Thomas M.
Durkin, John Keenan
Dyer, W. Wallace

Eads, John T.
Easby, Mary Hoskins
Edeiken, Joseph
Egoville, John W.
Ehrich, William E.
Eiman, John
Elfman, Louis Kenneth
**†Eliason, Eldridge L.
Ellis, Van Mashburn
Ellison, Richard T.
Ellson, J. Vernon
Ely, William C.
Engel, Gilson C.
English, O. Spurgeon
Erb, William H.
Estes, W. L., Jr.

Farell, David M.
Farr, Clifford B.
Farrar, George Elbert, Jr.
Farrell, John T., Jr.
Ferguson, Lewis Kraeer
Fetter, Ferdinand
Fetter, Theodore R.
Fewell, Alexander G.
Finkelstein, Arthur
First, Arthur
**Fitz-Hugh, Thomas, Jr.
Flexner, Louis B.
Flick, John B.
Flippin, Harrison F.
Fraley, Frederick
Friedman, Paul Sigmund
Friedman, Reuben
Fry, Kenneth E.
Fry, Wilfred Eyles
Furlong, Thomas F., Jr.

Gammon, Geo. D.
Garner, Vaughn C.
Geist, Donald C.
Gibbon, John H., Jr.
Gibson, Glen Gregory
Gifford, Edward S., Jr.
Gilman, Robert L.
Ginsburg, Isadore W.
†Goepp, R. Max
Goldberg, Samuel J.
Goldburgh, Harold L.
Goldsmith, N. Ralph
Gopadze, Illarion I.
Gordon, Burgess L.
**Grant, Francis Clark
†Greenbaum, Sigmund S.
Greene, Lloyd B.
Griffith, John Q., Jr.
Groff, Robert A.
Gross, Elmer R.
Guthrie, Donald

Gwyn, Norman B.
György, Paul

Hadden, Samuel B.
Hafkenschiel, Joseph H.
Harrison, William John
Harvey, Rolfe Marsh
Haskell, Benjamin F.
Hatfield, C. Alexander
Hawthorne, Herbert Reid
Hayman, Joseph M., Jr.
Herbut, Peter A.
Herman, Leon
Hewson, William
Heyl, W. Meredith
Hirst, John C.
Hirst, Otto C.
Hitschler, William J.
Hitzrot, Lewis H.
Hodes, Philip J.
Hoffman, George L., Jr.
Hollander, Joseph L.
Hopkins, Henry U.
Houser, Karl Musser
Hubbard, John P.
Hughes, Joseph
**Hughes, P. Boland
Husik, David N.

Imber, Irving
Israel, Harold L.
Israel, S. Leon
Ivy, Robert H.

Jacobs, Maurice
Janton, O. Henry, Jr.
Jeffers, William A.
**Johnson, Julian
Johnson, Thomas A.

Kaplan, Louis
Katz, G. Henry
**Kauffman, M. Luther
Kay, Calvin Frederick
Keeler, Harold R.
Keiserman, Joseph
Kelley, George F. J.
Kelly, Herbert T.
Kennedy, Patrick J.
**Kern, Richard A.
Keyes, Baldwin L.
Kimbrough, Robert A.
King, Orville C.
Kirshner, Jacob J.
Klauder, Joseph V.
Klein, Thomas
Kline, Oram R.
Klopp, John W.
Knowles, Frank C.
Kobler, H. B.
Kolmer, John A.
Koop, C. Everett
Kornblueh, Igho H.
Kramer, David W.
Kremer, David N.
Kressler, Robert J.
Krumbhaar, Edward B.
Kuhlenbeck, Hartwig

La Clair, Charles H., Jr.
Lame, Edwin L.
**Lamont, Austin
Lampe, William T.
Lansbury, John
Laplace, Louis B.
Laws, George M.
**Leaman, William G., Jr.
Learner, Norman
Lehman, James A.
Lehman, J. Stauffer
Leopold, Irving H.
Lhamon, William T.
Lisker, Samuel
Livezey, Mary M.
Livingood, Clarence S.
Loewenberg, Samuel A.
†Long, Charles-Francis
Long, Esmond R.
Long, Joan Humphrey
Longaker, Edwin P.
Lorber, Stanley H.
Lownes, John B.
Lucké, Balduin H. E.
Lukens, Francis D. W.
†Lull, Clifford B.
Luongo, Romeo A.
Lurie, Max B.
Lynch, Frank B., Jr.

McCahey, James F.
McCall, Milton L.
McCarthy, Daniel J.
**McClenahan, William U.
McCrea, Lowrain E.
McCutcheon, Morton
McDonald, P. Robb
McGavic, John S.

McMillan, Thomas M.
McPhedran, F. Maurice
†McReynolds, Robert P.
Macfarlane, Catharine
Machella, Thomas E.
MacNeal, Perry Scott
Mac Neish, W. J.
Maeder, LeRoy M. A.
Mann, Bernard
Margolies, Alexander
Martin, James R.
**Martin, William L.
Mason, James B.
May, Hans
Meade, Richard H., Jr.
Mendell, Theodore H.
Meranze, David R.
Middleton, William S.
Miller, Ford A.
Miller, Franklin R.
**Miller, T. Grier
Mohler, Roy W.
Montgomery, Hugh
Montgomery, John B.
Montgomery, Thaddeus L.
Moore, John Royal
Moore, Matthew Thibaud
Moorhead, Stirling W.
Morris, I. Paul
Mucklé, Craig Wright
Mudd, Stuart
Mullen, Carroll Richard

Naide, Meyer
Nardone, Anthony A.
Neese, Paul H.
Nelson, Guy M.
Newton, Zachariah B.
**Nicholson, Jesse Thompson
Nicholson, Samuel T.
Noone, Ernest L.
**Norris, George W.
Norris, Robert F.

O'Neal, Alexander Hay
O'Neill, James F.
Ornsteen, A. M.
Ornston, Darius Gray
Owen, Hubley R.

†Packard, Francis R.
Parker, Alan P.
Parkhurst, Leonard Woods
Payne, Franklin L.
Pearce, Louise
**Pendergrass, Eugene P.
Pepper, D. Sergeant,
Pepper, O. H. Perry
Percival, Milton Fraser
Perloff, William Harry
Pessel, Johannes F.
Pettit, Horace
Pettit, Mary DeWitt
**Pfahler, George E.
**Pfeiffer, Damon B.
Pfeiffer, Mildred C. J.
Phillips, Arthur W.
Piersol, George Morris
Pierson, Daniel B., Jr.
Pillsbury, Donald M.
Polk, David Stewart
Porter, Roland De Lance
Prickett, John A.
Putney, Floyd Johnson

Radbill, Samuel X.
Ramsey, Frank M.
Rathmell, Thomas K.
**Ravdin, I. S.
Reese, Warren S.
Reeves, Rufus S.
Rehfuss, Martin E.
Reiff, E. Paul
Reimann, Hobart A.
Reimann, Stanley P.
Reisinger, John A.
**Rhoads, Jonathan E.
Richards, James L.
Riesman, David (Fund)
Ritter, Joseph A.
Robbins, Frederick R.
Robertson, Harold F.
Robertson, William Egbert
Rose, Edward
Rose, Elizabeth Kirk
Rosemond, George Parrott
Rothman, Maurice M.
Rouse, George P., Jr.
Royster, Henry P.
Royster, Hubert A., Jr.
Rudolphy, J. Besson
Rupp, Charles
Rush, Alexander
Rynes, Samuel E.

**Sampson, David Alan
Saul, Leon J.
Sautter, Albert C.

Saÿen, John J.
Schaeffer, J. Parsons
**Scheffey, Lewis C.
**Scheie, Harold G.
Schlezinger, Nathan S.
Schnabel, Truman G.
Schulz, Norbert J.
Schwarz, Gabriel A.
Scott, T. F. McNair
**Section on General Medicine
Shallow, Thomas A.
Shands, Alfred R., Jr.
†Shanno, Ralph L.
Sharpless, Frederick C.
Shay, Harry
Shiffer, Paul H.
Shipman, James Shelby
Shuster, Benjamin H.
Sidlick, David M.
Silcox, Louis E.
Snodgrass, L. E.
Sokoloff, Martin J.
Soloff, Louis A.
**Sommer, George N. J.
Sommer, George N. J., Jr.
Spaeth, Edmund B.
Spangler, John Luther
Stadie, William C.
Starr, Isaac
Stecher, H. Armin
Stein, Irvin
Steiner, Charles A.
Stengel, Alfred, Jr.
Sterling, Julian A.
Stevens, Lloyd W.
Stiles, Merritt H.
Stockwell, Eunice L.
Stokes, John H.
Stokes, Joseph, Jr.
Stokes, S. Emlen
Strecker, Edward A.
Stroud, William Daniel
Strumia, Max M.
Stuckert, Harry
Sturgis, Margaret C.
Sturgis, Samuel Booth
Summey, Thomas J.
Swartley, William B.
Swenson, Paul C.

Tait, Edwin Forbes
Tassman, Isaac S.
Tauber, Robert
Taylor, Ann Gray
Thomas, J. Earl
Thompson, Charles M.
Thompson, Wesley D., Jr.
**Thorington, J. Monroe
Thornton, Mary Bickings-
Tocantins, Leandro Maués
Tompkins, Pendleton
Town, Arno E.
Trueman, Robert H.
Tuft, Louis
Tumen, Henry J.
Turman, Christopher M.
Turner, Creighton H.

Uhle, Charles A. W.
Ullom, Josephus T.

Vander Veer, Joseph B.
Van Loon, Emily Lois
**Vastine, Jacob H.
Vastine, Mary F.
Vaux, Norris W.
Veasey, Clarence A.
Vischer, Thomas J.

Wagner, Frederick B.
Wagner, Joseph A.
Waldman, Joseph
Walkling, Adolph A.
Watt, Charles C., Jr.
Weaver, Ruth H.
Weeder, S. Dana
Weidman, Fred D.
Weiss, Edward
Whelan, G. L.
Widmann, Bernard P.
Willard, De Forest
Willard, John Harrington
Willauer, George
†Williams, Horace J.
Williams, John C.
Williams, Philip F.
Willson, J. Robert
**Wilson, George
Wilson, Lucius R.
Wister, James W.
Wohl, Michael G.
Wolferth, Charles C.
Wolman, Irving J.
Wood, Alfred C.
Wood, Dorothy D.
**Wood, Francis C.
Wood, H. Curtis, Jr.

Wood, Oscar T.
†Woodward, George W.
**Wright, Carroll S.

Yaskin, Joseph C.

Young, Barton R.

Zeigerman, Joseph H.
Zentmayer, William
Zulick, J. Donald

Development Fund

**Aircraft-Marine Products, Inc.
Mr. Charles C. Alexander, Jr.

Mr. & Mrs. Frank Bachman
Mr. Benjamin Baldwin
Dr. J. H. Bisbing
Mr. Arthur Bloch
Dr. & Mrs. P. E. Bomberger
Mr. Charles M. Boswell
Mrs. E. L. Brady
Paul Brosz & Sons, Inc.
Mr. Richard P. Brown
Buckingham Mountain Foundation
Mr. Orville H. Bullitt
Dr. Thomas Butterworth

Campbell & Bro., Inc.
Mr. Charles E. Carr
Mrs. Harry B. Casselberry
Miss Rose H. Clark
Mr. Martin W. Clement
**Mr. Philip Cohen
Collins & Aikman Corp.
Mr. Nathaniel Cooper
Mr. Ralph Cornell

Dr. Arthur M. Dannenberg, Jr.
Mr. Richard Darlington
Mr. Charles E. Dearnley
Mr. Elmer Deaver
Anonymous Donors Obtained by A. F. DePalma (*Fellow*)
Mr. Gus Ditz

Mrs. Newbold Ely

**Fairmount Farm
Miss Helen C. Fannon
Anonymous Donor obtained by Ferdinand Fetter (*Fellow*)
Mr. I. B. Finkelstein
Mr. Percival E. Foerderer
Mr. Israel Forman
Mr. Samuel M. Freeman
Mr. N. E. Funk

Mr. Anthony S. Gaccione
Dr. Malcolm Z. Gearhart
Mrs. Joseph J. Geer
Mr. Arnold Gerstell
Mr. William Gerstley
Miss Mary K. Gibson
Mr. Morton Gittleman
Mr. Benjamin Glogow

**Mr. Otto Haas
Miss Anne Harbison
Miss Helen W. Harbison
Mr. Frank C. Hartzell
Mrs. Maurice Heckscher
Hess Brothers
High Production Machine Co., Inc.
Miss Mary A. Holland
Mrs. L. J. R. Holst
Mrs. Sarah D. Horstmann
Mrs. Edith L. Horter
Mr. Samuel P. Howe
**Mrs. Ralph B. Howland
Dr. Ralph C. Hoyt
Mr. & Mrs. Milton Hubschman

Mr. Arthur T. Ibbotson, Jr.
Infanta Knitting Mills

Mr. Charles M. Johnson

Mrs. Bayard Kane
Mr. Samuel Kasser
Mr. Edwin R. Keedy
Mr. Everett L. Kent
Miss Ellen C. Kerr
Mr. George M. Kerr
Charles B. Knox Gelatine Co., Inc.
Mrs. Harry E. Kohn
Mr. C. H. Krumbhaar
Mrs. E. B. Krumbhaar
Lankenau Hospital Research Institute
**Mr. Edwin M. Lavino
Dr. Howard M. Leinbach
Mrs. Agnes Yarnall LePage
Mr. John F. Lewis, Jr.
Mrs. Leicester S. Lewis
J. E. Limeburner Co.
Mrs. Rawson G. Lizars
Mr. Benjamin Loeb
Mr. & Mrs. Howard A. Loeb

Anonymous Donor obtained by Catharine Macfarlane (*Fellow*)
Mr. Samuel P. Mandell
Frederick R. Mann Foundation
Mrs. Helen Marshall
Dr. Edith A. Mayo
Anonymous Donor obtained by Milton L. McCall (*Fellow*)
Mr. John B. McClatchy
Mr. William L. McLean
**Mr. Robert Lincoln McNeil
Mr. John McShain
Mrs. Sarah G. Miller
Mrs. Grenville Dodge Montgomery
Abe Chas. Myers & Samuel Myers Foundation
Mr. Samuel Myers

Mr. Douglas T. Neale
Mr. Albert J. Nesbitt
Mrs. Rita D. Newbold
Messrs. Frank L., Jr., and Richard L. Newburger

Mr. William H. Oldach

**Palisades Foundation
Mrs. Francis D. Patterson
Mr. Henry N. Paul
Pennsylvania Range Boiler Co.
Dr. Charles S. Pennypacker
Philadelphia Orthopedic Club
Mr. & Mrs. Calvin L. Pontius
Precision Manufacturing Co.
Mr. Eli Kirk Price, 3rd
Mr. Philip Price

Mr. H. A. C. Rauchfuss
Mrs. C. L. Ritchie
Mr. Samuel Robinson
Mr. E. E. Rodenbough
Fred J. Rosenau Foundation
Mr. Lessing J. Rosenwald
Dr. F. G. Runyeon
Mrs. Louis Rush

Dr. M. H. Samitz
Edwin J. Schoettle Co.
Sears, Roebuck & Co.
Dr. Hyman I. Segal
Mr. Frank Seitchik
Mrs. S. Selig
Sentman Motor Co., Inc.
Mr. James O. Siegel
**Mrs. Florence Sayre Skinner
Mr. John Slater
Mr. & Mrs. Harry Snellenburg
Mr. & Mrs. D. Hays Solis-Cohen
Dr. Clair G. Spangler
Mr. Floyd T. Starr
Mr. Benjamin Steinberg
Mr. William G. Steltz
Mrs. S. Emlen Stokes
Stradley, Ronon, Stevens & Young
Sunshine Club
Supplee-Biddle-Steltz Co.
Mrs. E. H. Sutherland
Miss Jean Sutherland

Mrs. James E. Talley
Miss Emily G. Taylor
Mr. J. Kirby Tomkins
Towers, Perrin, Forster & Crosby, Inc.
Mr. Ernest T. Trigg
Dr. Frank Tropea, Jr.

United Engineers & Constructors, Inc.
Mr. Charles R. Wall
Mr. Ritner K. Walling
Dr. Leland F. Way
Mr. Charles N. Welsh, Jr.
Mrs. William B. Westcott
Mr. & Mrs. William White
Dr. Philip R. Wiest
Mrs. E. Burke Wilford
Mr. F. W. Wilkening
Dr. Gilbert Winston
Dr. John M. Wotring

York Lodge 266 F. & A. M.

Dr. Louis Zetzel
Dr. David E. Zion

James Harold Austin Memorial Fund

John H. Abbott
Charles R. Austrian
Rush C. Baumann
Robert B. Brown
William W. Cadbury
Alan M. Chesney
Eugene F. DuBois
Sylvan H. Eisman
Clifford B. Farr
Frederick Fraley
Paul S. Friedman
Joseph H. Hafkenschiel

Ralph K. Hollinshed
Howard J. Howard
O. Henry Janton
Richard A. Kern
Roger I. Lee
Paul B. Magnuson
J. P. Markley
J. H. Means
T. Grier Miller
Harold H. Morris
William L. Moss
H. H. Muhlenberg
F. W. Palfrey
John R. Paul
Pepper Laboratory (Technical Staff)
I. S. Ravdin
J. Parsons Schaeffer
Section on Medical History
H. T. Simmonds
Antonio G. Sison
C. Clyde Sutter
Leandro M. Tocantins
Karl M. Vogel
Joseph A. Wagner
Fred D. Weidman
Philip F. Williams
Woman's Medical College of Pennsylvania (Dept. of Med.)

Contributors to the Library

McNeil Laboratories
Merck & Co., Inc.
National Drug Co.
Sharp & Dohme, Inc.
Smith, Kline & French, Inc.
Wyeth, Inc.

TRANSACTIONS & STUDIES

of the

College of Physicians of Philadelphia

Volume 21 (Fourth Series)

Number 2 (August 1953)

The Evaluation of the Adaptation Concept in Relation to the Connective Tissue Diseases*

By WALTER BAUER, M.D.

Chief of the Medical Services, Massachusetts General Hospital; Jackson Professor of Clinical Medicine, Director, Robert W. Lovett Memorial Foundation for the Study of Crippling Diseases, Harvard Medical School, Boston, Massachusetts

I GREATLY appreciate the honor of having been invited to give the 1953 Musser Lecture. For me to extoll the many attributes of Benjamin Musser in whose memory this lectureship was founded would be like bringing coals to Newcastle. Therefore, without further ado, I shall turn to my chosen task of exploring another of medicine's partially charted seas—the role of the pituitary-adrenal axis in the causation of connective tissue diseases.

The human maladies that we have come to group together and speak of collectively as the collagen or connective tissue diseases are rheumatic fever, rheumatoid arthritis, disseminated lupus erythematosus, periarteritis nodosa, dermatomyositis and scleroderma. They are systemic in nature, variable in their manifestations and characterized by chronic inflammation of tissues of mesenchymal origin.

The concept of connective tissue disease was introduced by Klinge (1) in relation to rheumatic fever. His observation that the characteristic pathological changes of this disease are due to alterations in the fibrous connective tissue of the organs affected led him to postulate that fibrous connective tissue could be the site of primary disease. This reorientation of our views concerning the pathology of rheumatic fever, periarteritis nodosa and later rheumatoid arthritis provided the pathologist with the first plausible explanation of the widespread organ involvement seen in these diseases. This concept soon found application in the elucidation of other systemic diseases in which no common denominator had been found. Klemperer and his colleagues (2, 3, 4)

* Benjamin Musser Lecture IV, College of Physicians of Philadelphia, 7 January 1953. Publication No. 138 of the Robert W. Lovett Memorial Foundation for the Study of Crippling Diseases, Harvard Medical School, Boston, Massachusetts.

From the Medical Clinic of the Massachusetts General Hospital, the Department of Medicine, Harvard Medical School, Boston, and the Massachusetts Department of Public Health.

The expenses of this investigation have been defrayed in part by a grant from the Commonwealth Fund.

The tables and charts appear also in a paper by the author to be published in *Recent Progress in Hormone Research*, vol. 8, 1953. The publisher—Academic Press, Inc.—has courteously sanctioned their publication in this paper.

explained the systemic nature of disseminated lupus erythematosus in like manner. They, however, stressed the striking alterations in the collagenous portion of the fibrous connective tissue and coined the term, collagen disease. They were fully aware that the collagen changes were but one of the morphological characteristics of the underlying morbid disease process. In order to avoid further misinterpretation of their concept, we quote directly: "The term, collagen disease, was originally proposed to call attention to systemic alterations of the extracellular components of the connective tissue as a pathologic-anatomic feature common to a group of apparently heterogeneous diseases. It was not intended to use the term in a diagnostic sense, since it was realized that it referred to one morphologic characteristic only, and therefore obviously could not define the underlying morbid process of the diseases grouped together (3)." Because the term, collagen disease, implies that the changes are confined to collagen fibers, it is misleading. Since these diseases are characterized by alterations in the entire connective tissue complex, we prefer the term, connective tissue disease. Any inquiry into the mechanisms of these maladies must account for connective tissue alterations in addition to those observed in collagen.

Are these diseases well-defined entities as most textbooks would have you believe? Clinical experience soon teaches one otherwise. The variations in the clinical manifestations of any one of these diseases, whether judged at the time of onset or subsequently, can be so marked that accurate diagnosis is extremely difficult or impossible. At times, one may observe typical features of two or more of these diseases in the same patient. Occasionally, one of these diseases seems to supersede another. These similarities and overlaps are readily apparent when the clinical features of these diseases are presented in tabular form (see *Table I*). Thus one notes the polymorphic features of the connective tissue diseases. The many similarities suggest that these maladies may be related. However, the clinical resemblances are too superficial to permit this interpretation.

TABLE I

CLINICAL MANIFESTATIONS OF CONNECTIVE TISSUE DISEASE

The + sign indicates those findings seen with some regularity in a large series of patients, but implies nothing as to frequency or severity. The 0 signifies that this particular finding has been absent in our experience or cannot be attributed directly to the disease. The ± indicates an extremely rare finding. The frequency with which the leukocyte counts deviate from normal (N) is indicated grossly by the size of the arrows ↑ = leukocytosis, ↓ = leukopenia.

	CONSTITUTIONAL	VASOMOTOR	CHOREA	OCULAR	SKIN	PURPURA	MUCOUS MEMBRANES	LYMPHADENOPATHY	SEROSITIS	CARDIAC	HYPERTENSION	PULMONARY	GASTRO INTESTINAL	ARTHRITIS	NODULES	MUSCLES	PERIPHERAL NERVES	EOSINOPHILIA	RENAL	W.B.C.
RHEUMATOID ARTHRITIS	+	+	0	[+]	+	+	0	+	+	+	0	0	0	[+]	[+]	+	+	+	☺	↑
RHEUMATIC FEVER	+	±	[+]	±	+	+	0	0	+	[+]	0	+	+	[+]	[+]	☺	0	0	±	↑
LUPUS ERYTHEMATOSUS DISSEMINATUS	+	+	±	±	[+]	[+]	[+]	+	[+]	[+]	+	+	0	+	[+]	+	0	0	[+]	↓
PERIARTERITIS NODOSA	+	±	0	0	+	+	0	+	+	+	[+]	+	+	+	+	[+]	[+]	[+]	[+]	↑
DERMATOMYOSITIS	+	+	0	0	[+]	±	±	+	±	±	0	0	[+]	+	+	[+]	0	+	±	↑
SCLERODERMA	±	+	0	0	[+]	0	0	0	0	+	0	+	[+]	+	0	+	0	0	0	N

The distinguishing clinical features of the connective tissue diseases are presented in *Table II*. Here one notes that these maladies usually conform to distinct disease patterns.

Time will not permit the presentation of

case reports to illustrate instances in which one disease seems to supersede another or examples of clinical and pathologic overlaps. That they can occur would be clearly evident if we reviewed specific case records in detail. More important is the question of the possible relationship of one disease to another. These coined labels, which imply disease identification, though helpful to the clinician, may be misleading in interpreting the true nature of these systemic diseases which have a predilection for fibrous connective tissue. It may be that differences in host and tissue responses to an X factor can account for the very common, yet at times, similar clinical picture seen in this group of human maladies. However, such an interpretation is mere conjecture.

It is generally agreed that these diseases are characterized by widespread changes in the morphology and staining properties of the connective tissue, although each disease presents certain distinctive features. When all features are present, and the lesions are distributed in a characteristic fashion, the identity of these diseases can usually be established.

In general, three distinct characteristics are observed. They are: (1) Degeneration including fibrinoid change, (2) proliferation and (3) inflammatory reaction. The distribution of the lesions in organs is of importance in characterizing these diseases. Each entity has a characteristic systemic distribution of the inflammatory lesions which determines its clinical features and functional impairment. Although lesions are widespread, we recognize the joints to be primarily involved in rheumatoid arthritis, the heart in rheumatic fever, the skin in scleroderma, and the muscles and skin in dermatomyositis. Although the lesions of lupus erythematosus disseminatus and periarteritis nodosa are more diffuse, certain organs are involved more frequently.

The intimate relationship of these connective tissue lesions to the blood vessels is striking. Except for the diffuse lesions of serous membranes, extravascular foci are most frequently in proximity to a vessel wall. This proximity of extravascular lesions to vessels and the actual involvement of the vessel wall raises the question of the presence of a humoral agent of pathogenic significance. Such an agent has never been identified.

The histologic changes observed in this group of diseases may also be present in serum sickness, thromboangiitis obliterans, malignant nephrosclerosis and glomerular nephritis. The presence of similar histologic changes in serum sickness and some inflammatory diseases of unknown etiology indicates that primary involvement of connective tissue is not limited

TABLE II

The symbols in this table are the same as in Table I except for the addition of squares. The latter signify the distinguishing features of each disease.

	CONSTITUTIONAL	VASOMOTOR	CHOREA	OCULAR	SKIN	PURPURA	MUCOUS MEMBRANES	LYMPHADENOPATHY	SEROSITIS	CARDIAC	HYPERTENSION	PULMONARY	GASTRO INTESTINAL	ARTHRITIS	NODULES	MUSCLES	PERIPHERAL NERVES	EOSINOPHILIA	RENAL	W.B.C.
RHEUMATOID ARTHRITIS	+	+	O	+	+	+	O	+	+	+	O	O	O	+	+	+	+	+	⊕	↑↓
RHEUMATIC FEVER	+	±	+	±	+	+	O	O	+	+	O	+	+	+	+	⊕	O	O	±	↑
LUPUS ERYTHEMATOSUS DISSEMINATUS	+	+	±	±	+	+	+	+	+	+	+	+	O	+	+	+	O	O	+	↓
PERIARTERITIS NODOSA	+	±	O	O	+	+	O	+	+	+	+	+	+	+	+	+	+	+	+	↑
DERMATOMYOSITIS	+	+	O	O	+	±	±	+	±	±	O	O	+	+	+	+	O	+	±	↑
SCLERODERMA	±	+	O	O	+	O	O	O	O	+	O	+	+	+	O	+	O	O	O	N

to the maladies herein designated connective tissue diseases. The common denominator of the latter diseases is a morphological one.

It has been postulated by Selye (5, 6, 7) that these diseases represent pathogenic situations in which the endocrine status plays a decisive role by virtue of a non-specific, stereotyped reaction to prolonged stress, involving principally the anterior pituitary glands and the adrenal cortex. The question to be considered is whether the repercussions of prolonged stress are intimately related to the connective tissue diseases. Be they related or not, Dr. Selye's many contributions have enhanced the sum total of medical knowledge, especially our understanding of endocrine, homeostatic and adaptative mechanisms. In interpreting the phenomena observed during stress, he has skillfully interwoven many apparently unrelated threads in an attractive and unique manner. Many of the theoretical considerations have been the subject of considerable controversy and criticism. This, however, has not been without benefit for it has served to stimulate investigation in many of the medical sciences which otherwise might not have been undertaken. Whether or not Dr. Selye's concept of diseases of adaptation is right, it has awakened or revived the interest of many in—the dynamics of illness and its many component parts—disease susceptibility—the polymorphic nature of disease—the possibility that seemingly heterogeneous disease states may represent common pathogenic situations—and other facets of illness. His concept, if correct, would not be without its preventive and therapeutic implications.

My chosen task is not an easy one in that it necessitates evaluation of an unproved etiologic concept which has been applied to a seemingly heterogeneous group of human diseases. The task is further complicated by the fact that the combination of conditions of the rat experiments upon which this etiologic concept is based is rarely, if ever, encountered in humans.

Although Dr. Selye would agree that the normal function of the anterior pituitary-adrenal cortex axis* is to maintain homeostasis, he postulates that during prolonged non-specific stress, these functions go askew. This maladaptation to stress, he believes, represents a permanent derailment of the pituitary-adrenal axis which causes a number of frequently occurring human maladies including the so-called collagen diseases (8).

Since the adaptation concept is difficult to perceive in its entirety, we shall review briefly the manner in which we have interpreted it. Selye describes the general adaptation syndrome as the sum of all non-specific, systemic reactions of the body which ensue upon long-continued exposure to stress.

The syndrome is divided into three stages: the alarm reaction, the stage of resistance and the stage of exhaustion. It is during the stage of resistance and exhaustion that hormones are elaborated, which has been postulated to have a basic etiologic relationship to certain diseases in man. Unfortunately, little is known about hormone production in the stages of resistance and exhaustion.

Selye originally postulated that diseases of adaptation were due to hyperactivity of the adrenals. In support of this concept, he reported the production of hypertension, nephrosclerosis and adrenal enlargement in unilaterally nephrectomized rats on exposure to cold, forced exercise and formalin (9). Subsequently, it was found that hypertension, nephrosclerosis, periarteritis nodosa-like lesions, Aschoff bodies and transient arthritis could be induced in unilaterally nephrectomized rats given an abnormally high sodium load and desoxycorticosterone acetate prior to exposure to cold. The overlapping of the lesions observed in these two types of experiments led him to postulate that certain diseases, including the rheumatic diseases, could be due to an excessive production of electrolyte hormone during stress.

He also noted that similar morphologic lesions could be induced in non-adrenalectomized rats with lyophilized anterior pituitary

* Hereafter, we shall use the term, pituitary-adrenal axis.

material. The pathogenicity of LAP was attributed to a corticotrophic effect with the production of an excess of electrolyte hormone by the adrenal cortex. The discovery of the antirheumatic effects of corticotrophin made revision of this hypothesis necessary. In view of the similar antirheumatic effects of corticotrophin and cortisone, it was concluded that corticotrophin predominantly effects the production of carbohydrate-active steroids (glucocorticoids-Selye). Since lyophilized anterior pituitary powder caused adrenal enlargement, it was considered to contain corticotrophin. It was then postulated that an X factor was responsible for the production of an electrolyte hormone (mineralocorticoid-Selye). Thus developed the concept that purified corticotrophins were predominantly glucocorticotrophic and the X factor of LAP was predominantly mineralocorticotrophic. At this point, the terms, antiphlogistic (AC) and prophlogistic (PC) were introduced to indicate the predominant effect of the carbohydrate-active and salt-active corticoids in relation to inflammation. Subsequently, Selye observed that the somatotrophic hormone (STH) produced similar lesions to those induced by LAP and concluded that STH was the X factor. Because lesions appeared more readily with STH and DCA combined, he further assumed that STH sensitized the tissues to the latter. Additional experimental evidence of the prophlogistic effects of DCA and the antiphlogistic effects of cortisone were obtained from studies relating to the effect of these agents on formalin arthritis (9).

The adaptation concept depicted in the schematic diagram (*Figure I*) is taken from Dr. Selye's 1952 book on stress (8). From this, we understand that a pituitary factor X is liberated following stress and that this agent can produce morphologic lesions. The X factor is presumably STH. Its pathogenicity is attributed to its ability to produce an excess of mineralocorticoids or a disturbance in the ratio of mineralocorticoids to glucocorticoids, an increased tissue sensitivity to mineralocorticoids, including the hypothetical situation where tissues react to glucocorticoids as though they were mineralocorticoids.

The ability to produce lesions with DCA, LAP and STH that resemble those seen in human connective tissue disease led to the concept that alterations in anterior pituitary and adrenal cortical functions during prolonged stress play a key role in the production of these diseases.

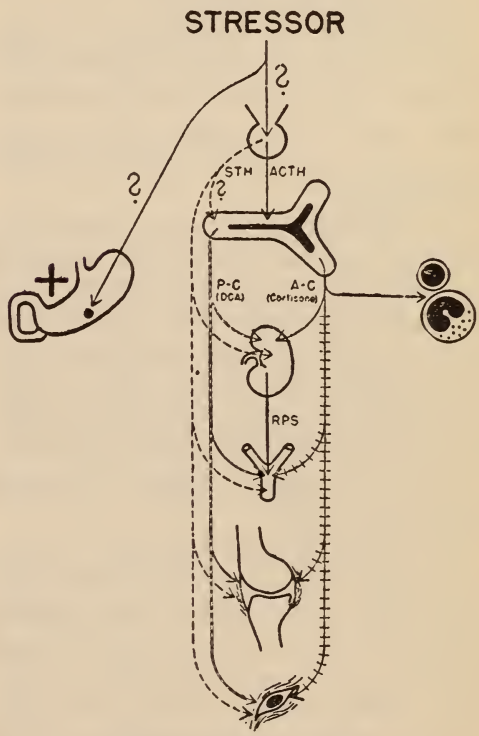

FIGURE I. SELYE DIAGRAM.

This schematic drawing indicates Dr. Selye's concept of the events that may transpire during prolonged stress. (Selye, H. The Story of the Adaptation Syndrome, Acta Inc., Montreal, 1952.)

On the basis of the information presented thus far, it is apparent that these diseases are grouped together because of one common denominator, namely, involvement of the fibrous connective tissue in various parts of the body. Though this concept facilitates our understanding of their clinical similarities, it does not permit one to conclude that these diseases are due to a common pathogenic mechanism. In all the diseases in this category

except those cases of periarteritis nodosa due to hypersensitivity reactions, the etiology is unknown. All etiologic theories proposed prior to the advent of Selye's concept of diseases of adaptation were without proof. Dr. Selye's theory—that the connective tissue diseases are pathogenic situations due to maladaptation to stress—if correct, would permit the possibility of many etiologic agents inciting a common pathogenic mechanism.

Evaluation of this comprehensive concept requires examination of the evidence and assumptions upon which it is based. On this occasion, time will not permit review of the experimental evidence upon which Dr. Selye's concept is based.

It is sufficient to state that even if the genesis of connective tissue lesions in animals were established, their pathogenic relationship to human lesions could not be proved on the basis of morphology alone. This being true, I shall attempt to determine whether a significant relationship between experimental conditions and human disease exists. If so, the concept of adaptation diseases in humans would be more valid.

Do the experimental conditions essential for the production of the rat connective tissue disease occur in man and are they regularly associated with any of the connective tissue diseases? Man is certainly subject to stress, he may suffer from an excess of growth hormone, he has unilateral nephrectomy, his salt intake may vary and he is given DCA with or without functioning adrenals. If these conditions are pathogenically related to human connective tissue disease, one should expect to encounter them with some regularity.

Knowledge of rheumatic fever and rheumatoid arthritis exceeds that of the other connective tissue diseases and our own experience is most extensive with rheumatoid arthritis. Hence, our comments will pertain chiefly to this disease.

Stress

Reliable data on the exact relationship of stress to these diseases is not available. The frequent occurrence of streptococcal infections preceding rheumatic fever suggests a specific relationship. However, rheumatic attacks are preceded by a variety of non-specific stresses. What process is initiated under these circumstances is not known. Acute attacks of lupus erythematosus disseminatus and dermatomyositis have been noted to appear following exposure to excessive amounts of sunlight. This apparently specific sensitivity may be related to a specific metabolic defect in porphyrin metabolism. Periarteritis nodosa has resulted from the administration of horse serum, sulfonamides and other medicaments. Such instances have been attributed to hypersensitivity to the specific noxious agent concerned. The recorded incidence of other precipitating factors in these three diseases is too incomplete to relate them to non-specific stress.

It is the impression of most clinicians that rheumatoid arthritis can be precipitated and unfavorably influenced by stress. Studies by Short *et al.* have shown that approximately 50 per cent of 293 patients with rheumatoid arthritis associated the onset of their disease with a wide variety of stresses (10). A number of these patients gave a history of two or more stresses; the most common combination was emotional strain of long duration with the onset immediately preceded by an infection, operation or injury. Such studies are hampered by inability to date the onset of the disease. Observations thus far suggest that stress is in some way related to these diseases.

Pituitary Disturbances

The appearance of rheumatoid arthritis in association with panhypopituitarism has been reported (11), indicating that a pituitary hormone is not essential for the development of this disease. The manifestations of connective tissue diseases are not associated with acromegaly, an endocrinopathy due to an excess of growth hormone.

Wetzel has reported retardation of growth in rheumatic fever (12). It is of interest that the period of growth "idling" coincided with the elevation of the sedimentation rate. Dwarf-

ism has been observed in children with rheumatoid arthritis. The exact nature of growth impairment is not known. The thesis that an excess of growth hormone is a feature in the connective tissue diseases cannot be supported by clinical observations.

Adrenal Function

The persistence of rheumatoid arthritis in a patient developing Addison's disease, reported by Perera and Ragan, indicates that an adrenal hormone is not essential for the maintenance of the former and also suggests that adrenalectomy would be without a favorable effect on rheumatoid arthritis (13). They observed that 25 mgm. of cortisone per day were as effective as 100 mgm. DCA administered on two occasions in doses of 2 and 4 mgm. per day did not antagonize the antirheumatic effect of either dose of cortisone. The severity of the arthritis was not increased when only DCA was given.

The appearance of arthralgia during the administration of DCA to patients with Addison's disease has been reported (14). However, there have been no pathologic studies reported indicating that DCA in such instances actually induces arthritis or connective tissue lesions. We have observed a group of patients falling in this category but have found objective evidence of inflammatory joint disease in only three of the cases. All the latter patients had had rheumatoid arthritis prior to the onset of Addison's disease. Although exacerbations occurred while DCA pellets were in place, we could not relate these exacerbations to the administration of DCA.

The range of excretion of urinary 17-ketosteroids, glucocorticoids and formaldehydrogenic steroids has been reported by Venning *et al.* to be lower in rheumatoid arthritics than in normals (15). From these and Dobriner's studies on steroid hormone metabolites, it would appear that rheumatoid arthritics as a group have a lowered adrenal function. It is of interest that Venning *et al.* found high urinary glucocorticoid (by biologic assay) values in three patients with rheumatoid arthritis during an acute phase of the disease. Steroid excretion studies of this type, however, do not preclude the existence of an excess of an electrolyte hormone as postulated by Selye.

Abnormalities of urinary steroid patterns as reported by Dobriner (16) (17) and also by Engel *et al.* (18) suggest adrenal dysfunction, but such data are not at the moment applicable to the adaptation concept. Furthermore, it has not yet been established whether the adrenal dysfunction suggested by their data is of pathogenic significance or merely incidental to severe systemic disease.

Mineralocorticoid Activity

We have been unable to demonstrate a significant anomaly in the behavior of electrolytes in rheumatoid arthritis. Many patients have been found to have slight lowering of serum sodium concentrations with normal serum potassium concentrations. In one such patient, a salt load neither corrected the serum sodium abnormality nor altered the arthritis.

We have observed no significant anomalies in electrolyte balances in six patients with rheumatoid arthritis studied on the metabolic ward. Data from eleven experiments on this group are presented in *Figure II*. The sodium, potassium and chloride balances were positive in all experiments. The mean daily sodium balance ranged between +7.2 and +18 meq. The mean daily potassium balance ranged between +0.9 and 13.6 meq. The mean daily chloride balance ranged between +2.5 and 30.9 meq. The positive balances correspond to electrolytes lost through sweating and cannot be interpreted as indicating excess of "salt-active" hormone.

Robinson (19) studied ten patients with rheumatoid arthritis by Conn's method (20) of establishing the concentration of electrolytes in thermal sweat as an index of adrenal cortical function. He found higher levels of sweat sodium and chloride in these patients than had been found by Conn in normals. His observations give additional evidence against an overproduction of mineralocorticoids which

would have resulted in values in the hyperadrenalism range.

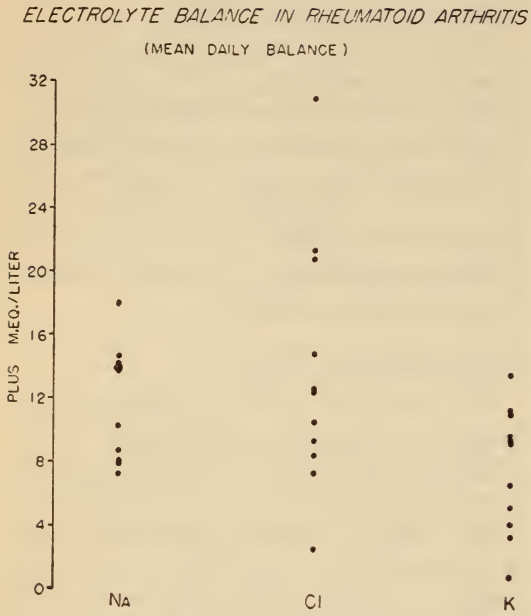

FIGURE II. MEAN DAILY ELECTROLYTE BALANCES DURING CONTROL PERIODS IN 11 EXPERIMENTS PERFORMED ON 6 PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS.

diseases are associated with a relative or absolute deficiency of glucocorticoids. Studies of Venning *et al.*, already referred to, are not entirely consistent with this thesis because of the exceptions mentioned. Although an absolute decrease in the production of carbohydrate-active steroids is likely in many if not all of these diseases, it cannot be considered of primary etiologic significance, since it can now be corrected by substitution therapy. A relative deficiency of this steroid from increased utilization or metabolic inactivation cannot be precluded by studies thus far. Decreased glucose tolerance, frequently observed in rheumatoid arthritis, is not consistent with a glucocorticoid deficiency.

Effects of Desoxycorticosterone

The administration of DCA (desoxycorticosterone acetate) and DCG (desoxycorticosterone glucoside) does not alter the manifestations of rheumatoid arthritis nor does it unfavorably influence the antirheumatic effects of cortisone. We have studied one patient extensively in this regard while on the metabolic ward receiving cortisone, DCA and testosterone singly, together and in binary combinations. This study (illustrated in *Table*

TABLE III

From this table it is apparent that desoxycorticosterone acetate was without effect on the patient's rheumatoid arthritis when administered alone or in combination with testosterone and that no antagonistic effect was noted when it was given with cortisone or cortisone and testosterone.

TREATMENT (mgms/day)			DURATION	NA INTAKE	NA BALANCE	WEIGHT CHANGE	CHANGE IN ARTHRITIS
CA	DCA	TS*					
			Days	*meq/period*	*meq/period*	*Kg.*	
150	—	—	12	777.6	−16.47	−0.62	Imp. +++
—	25	—	8	480.0	+120.9	+1.04	0
—	—	100	8	528.0	+53.8	+1.42	0
150	25	—	8	480.0	+136.8	+0.35	Imp. +++
150	—	100	8	528.0	+43.5	+1.50	Imp. +++
—	25	100	8	480.0	+172.6	+2.50	0
150	25	100	8	480.0	+158.2	+1.80	Imp. +++

* CA Cortisone Acetate
DCA Desoxycorticosterone Acetate
TS Testosterone Suspension

Glucocorticoid Activity

The favorable effects of cortisone in connective tissue diseases have suggested that these

III) was designed to determine the influence of these agents on the manifestations of active rheumatoid arthritis and to correlate changes in the disease with mineral and nitrogen balances. Desoxycorticosterone was administered in the form of the acetate in the dosage of 25 mgm. per day intramuscularly. Cortisone acetate was administered in the dosage of 150 mgm. per day and testosterone suspension was given in the dosage of 100 mgm. per day. It was found that desoxycorticosterone acetate did not increase the manifestations of inflammatory activity when administered alone. It was also observed that it did not alter the clinical response to cortisone. Both DCA and testosterone produced considerable sodium

TABLE IV

Desoxycorticosterone glucoside (DCG) in doses of 100 to 150 mgm. per day was without effect on the rheumatoid arthritis of four patients during the time of administration or subsequently.

PATIENT	HORMONE	DOSE	DURATION	CHANGE IN ARTHRITIS	WEIGHT GAIN
		mg/24 hr.	*Days*		
E. M.	D.C.G.	100	17	0	0
S. K.	D.C.G.	100	7	0	6 Kg.
M. M.	D.C.G.	100	4	0	2 Kg.
W. G.	D.C.G.	100	4	0	0
W. G.	D.C.G.	150	12	0	0

retention, whereas sodium retention under the influence of cortisone was minimal and when sodium balances during cortisone were corrected for control values, a net loss was shown. The administration of desoxycorticosterone and cortisone together resulted in considerable sodium retention with sodium diuresis occurring immediately upon cessation of therapy. The characteristic hormone-induced improvement occurred during the period of sodium retention, and the patient relapsed during the period of sodium diuresis. There seemed to be no relationship between clinical response and sodium retention.

Experiments were performed on four patients with typical, active rheumatoid arthritis in which desoxycorticosterone glucoside was administered in doses of 100 to 150 mgm. per day (see *Table IV*). Duration of the medication was 4 to 17 days. All patients were maintained on strict low sodium diets. However, no balance measurements were made. No one of these patients experienced any objective change in the severity of their rheumatoid arthritis during these experiments or subsequently. Although the dosages of DCA and the salt intake used in rats could not safely be given to the patients, these observations are contrary to the thesis that salt hormone plays a role in rheumatoid arthritis.

Effects of Cortisone

If an altered ratio between carbohydrate-active and salt-active steroids is significant in the pathogenesis of connective tissue diseases, one would suspect that the administration of the former should invariably be associated with measurable improvement of a significant degree. However, the administration of ACTH and cortisone even in large doses may have very little or no effect in certain of these diseases, even though hypercorticism is induced. We have observed the ineffectiveness of cortisone in dermatomyositis and scleroderma in patients with relatively early progressive disease. Although a dramatic response is usually observed in rheumatoid arthritis, an occasional patient may exhibit no significant subsidence of the objective signs of inflammation, though the dose of cortisone employed causes hypercorticism. As has been stated previously, the antirheumatic effect of cortisone was not antagonized by DCA in our studies or in the patient with Addison's disease reported by Perera and Ragan.

Conditioning Factors

We have observed no significant relationship between nephrectomy or salt intake and rheumatoid arthritis. Although renal involvement is essential to rat connective tissue disease produced by Selye, it is not recognized as a manifestation of rheumatoid arthritis. The arthritis of the patient with Addison's disease

was not altered by a salt intake exceeding 40 grams per day with or without the administration of DCA.

Though these observations on patients with connective tissue disease are not as extensive as might be desired, they do not support the concept that the experimental conditions of rat connective tissue disease play a role in the production of human disease. Perhaps we have overlooked some observations which are more favorable.

Discussion

In thinking of the etiology and pathogenesis of the connective tissue diseases, it must be borne in mind that the fibrous connective tissue may react in a similar way to many different types of injury and only the final step or steps in the chain of pathogenic cause and effect need be similar to account for the morphologic resemblance of the lesions. Nevertheless, the possibility of a common pathogenic mechanism still exists and should be entertained in any comprehensive investigative approach to the connective tissue diseases.

Dr. Selye's suggestion that an endocrine imbalance can play a basic etiologic role in these diseases is based on the similarity of the widespread inflammatory lesions in the fibrous connective tissue in the man-induced rat disease to those seen in the naturally-occurring human diseases.

Dr. Selye agrees that the normal function of the pituitary-adrenal axis is to maintain homeostasis, but he assumes that during prolonged non-specific stress this function can go askew. He believes that this maladaptation to stress represents a derailment of the pituitary-adrenal axis and some type of desoxycorticosterone intoxication which plays a basic etiologic role in the connective tissue diseases.

There is, however, no evidence that either normal animals or humans develop connective tissue diseases because of a hypersecretion or an imbalance of certain pituitary and adrenal cortex hormones in consequence of prolonged non-specific stress. There are reports that rats which have been sensitized by unilateral nephrectomy and a high sodium intake may develop connective tissue diseases when subjected to cold, forced exercise or formalin injections. However, no supporting experimental data are presented, nor has it been shown that any severe form of stress can cause such changes in connective tissue. All are agreed that any form of stress can cause tissue damage, but it remains to be demonstrated that human connective tissue diseases are caused in this manner.

There can be no doubt that the pituitary-adrenal axis is essential for the maintenance of certain diseases. This has been clearly shown in the case of both experimental diabetes and hypertension. However, the amelioration of these diseases by adrenalectomy does not permit the conclusion that these diseases are due to overactivity of the adrenals. The adrenal cortical hormones may play a similar "permissive" role in the manifestations of the connective tissue diseases, but there is no evidence to indicate that they play an etiologic role.

Despite the foregoing statements, it still must be admitted that DCA facilitates the production of connective tissue disease in the rat by the Selye technique. Whether it is the inciting agent responsible for the rat lesions produced by the administration of LAP and STH remains to be proved.

There is some evidence to indicate that DCA augments chemically-induced inflammation of connective tissue. However, there are no recorded observations to support the thesis that desoxycorticosterone exerts a diametrically opposite effect to cortisone in the case of human disease. DCA alone, in the dosage administered, does not augment the inflammatory process of rheumatoid arthritis, nor is there any direct evidence that DCA alone can cause inflammation of connective tissue.

The recorded observations, however, leave little doubt that the administration of DCA to properly conditioned rats can cause modification of connective tissue reactions characterized by inflammation and fibrosis. In consequence, there result widespread inflammatory lesions

of the myocardium, kidney and vascular system and at times an associated synovitis. Whether the synovitis is a manifestation of the experimentally-induced rat connective tissue disease is open to considerable question. It is transitory in nature and seemingly has been observed with equal, if not greater, frequency in DCA overdosage experiments on intact rats. The histological appearance is consistent with that of infectious arthritis. However, bacteriological examinations for saphrophytic organisms common to rats which might become pathogenic under the conditions of Selye's experimental study have not been reported. If the manifestations of this man-made rat disease are limited to the myocardium, kidney and vascular system, then we are probably dealing with an experimentally-induced periarteritis nodosa, a pathological entity, which has been produced by a variety of experimental methods.

It is unknown whether the biochemical and tissue changes of the lesions produced by Selye are the same as those occurring in human disease. The experimental conditions necessary for the production of the adaptation diseases are man-made. They are rarely if ever naturally-occurring states in either the rat or human.

The fact that the lesions observed by Selye are strikingly similar to those of periarteritis nodosa produced by other experimental methods raises certain questions concerning the pathogenesis of the former. Is Dr. Selye's strain of rat more prone to develop periarteritis nodosa than other strains? Do the conditions of the experiment (unilateral nephrectomy, high sodium intake and the administration of DCA) favor saphrophytic organisms becoming pathogenic? Does the experimental procedure favor the production of some type of hypersensitivity even though DCA is non-antigenic? Is a renal humoral factor (renal insufficiency and a high sodium intake) a prerequisite for the induction of these lesions by DCA? Could these experimental diseases be due to: reactivation of a latent virus, a non-specific allergic response, an increase in the titer of autoantibodies to some constituent of connective tissue? Unfortunately, these questions cannot be answered. Until the nature of the pathogenic mechanism is known, the exact etiologic role of DCA cannot be established. Once the latter has been determined, it will still be necessary to establish whether a predominantly salt-active steroid is a naturally-occurring adrenal hormone and whether it or some other salt-active hormone plays a basic role in the pathogenic mechanism or mechanisms of the group of heterogeneous human maladies classed as connective tissue diseases.

Concluding Remarks

The diseases included in the collective term, connective tissue diseases, though usually different in clinical pattern and prognosis, have certain features in common, the most striking of which are the alterations noted in the fibrous connective tissue of various organs. In an occasional case, both the vascular and the extravascular lesions are characteristic of two or more of the diseases included in this group. These isolated cases naturally suggest the possibility that these seemingly heterogeneous and distinct disease states might share a common pathogenic mechanism; their varied clinical manifestations being due to individual host and tissue susceptibility. No one of the common pathogenic theories proposed in the past has been substantiated except that of hypersensitivity in one of these diseases, experimental and human periarteritis nodosa.

Selye's comprehensive concept of diseases of adaptation merits consideration because it includes the diseases of the connective tissue as pathogenic situations or instances of tissue alterations as manifestations of permanent derailment of the pituitary-adrenal axis occurring during prolonged non-specific stress. The conditions of the experiment, upon which the theory is based, imply an endocrine imbalance with a salt-active corticoid as the agent playing a basic etiologic role. There is, however, no direct evidence in favor of the thesis that prolonged non-specific stress causes an-

terior pituitary-adrenal cortex hormonal imbalance resulting in mineralocorticoid intoxication in the diseases under consideration.

REFERENCES

1. Klinge, F.: Beitr. path. Anat. u. allgem. Path. **83:** 185, 1929; Ergeb. allgem. Path. u. path. Anat., Bd. 27, 1933.
2. Klemperer, P.: Am. J. Path. **26:** 505, 1950.
3. Klemperer, P.: Am. J. Med. **10:** 405, 1951.
4. Klemperer, P., Pollack, A. D., and Baehr, G.: J.A.M.A. **119:** 331, 1942.
5. Selye, H.: J. Clin. Endocrinol. **6:** 117, 1946.
6. Selye, H.: The physiology and pathology of exposure to stress. Montreal, Acta, Inc., 1950.
7. Selye, H.: Brit. M. J. **2:** 1129, 1949.
8. Selye, H.: The story of the adaptation syndrome. Montreal, Acta, Inc., 1952.
9. Selye, H.: Brit. M. J. **1:** 263, 1951.
10. Short, C. L., Abrams, N. R., and Sartwell, P. E.: In: Rheumatic diseases. Based on the proceedings of the seventh International congress on rheumatic diseases, p. 47. Phila., Saunders, 1952.
11. Schrock, C. E., Sheets, R. F., and Bean, W. B.: J. Clin. Investigation **30:** 174, 1951.
12. Wetzel, N. C.: J. Pediat. **22:** 208, 1943.
13. Perera, G. A., and Ragan, C.: Proc. Soc. Exper. Biol. & Med. **75:** 99, 1950.
14. Kepler, E. J., Sprague, R. G., Mason, H. L., and Power, M. H.: Recent Progr. Hormone Research **2:** 345, 1948. New York, Academic Press.
15. Venning, E. H., Johnson, L. G., and Rose, B.: In: Proc. Second Clin. ACTH Conf., p. 49. N. Y., Blakiston, 1951.
16. Dobriner, K.: In: Symposium on steroids in experimental and clinical medicine, p. 130. Phila., Blakiston, 1951.
17. Dobriner, K.: Bull. Rheumat. Dis. **2:** 5, 1951.
18. Engel, L. L., Lance, M., Ekman, G., Spaulding, K. H., Carter, P., and Nathanson, I. T.: In: Ciba foundation colloquia on endocrinology **2:** 274, 1952. London, Churchill.
19. Robinson, W. D.: Ann. Rheumat. Dis. **10:** 488, 1951; Proc. second Clin. ACTH Conf., p. 63. N. Y., Blakiston, 1951.
20. Conn, J. W.: Arch. Int. Med. **83:** 416, 1949.

Epidemiologic and Clinical Studies on Brucellosis, 1937-1952*

By WESLEY W. SPINK, M.D.

Professor of Medicine, University of Minnesota Medical School, Minneapolis, Minnesota

I FEEL deeply honored in being invited to give this James M. Anders Lecture. In preparing for this occasion, I have attempted to become acquainted with Dr. Anders by browsing through the Transactions of the College of Physicians of Philadelphia. I found that for almost a half century, ending with his death in 1936, he was an active participant in the discussions of this College. Although Dr. Anders was primarily a clinician, he was vitally interested in the formative days of public health and preventive medicine, and pleaded for a better understanding of diseases associated with certain occupations. I also discovered that on many occasions he concerned himself with the epidemiologic aspects of human illness, even including the problem of noise abatement in a large metropolitan area. And so, this evening, it is appropriate that as a clinician, I should invite your attention to the epidemiologic and clinical aspects of an occupational disease which has absorbed the interest of my associates and myself over a period of fifteen years. At present, of more than the 100 diseases of animals transmissible to man, brucellosis causes more human illness than any other.

The Etiology and Reservoir of Brucellosis

There are two basic features of brucellosis that are of considerable aid in comprehending the epidemiology and clinical aspects of human brucellosis. First, there are three species or variants of Brucella responsible for the disease in animals and in man, *Brucella melitensis*, *Brucella suis*, and *Brucella abortus*. Second, the reservoir for Brucella is in farm animals and livestock, particularly goats, sheep, hogs and cattle. Unfortunately for man, Brucella organisms in animals localize in the udder, and also in the reproductive organs, especially the pregnant uterus and in the testes. Brucellosis is very rarely transmissible from human to human.

Bruce (1) first isolated and identified *Br. melitensis*, and the classic investigations of the Mediterranean Fever Commission (2) demonstrated that man contracted the disease through the ingestion of contaminated goat's milk and milk products. In another classic monograph, Cantaloube (3), a French general practitioner, pointed out as early as 1911 that human beings were infected not only by drinking goat's milk, but also by contact with infected animals. He stated that the organisms entered the body through the skin. From experimental investigations carried out in our laboratory by Braude (4), and clinical observations that I have made in Mexico and in the littoral countries of the Mediterranean, *Br. melitensis* causes a more severe toxemia than that due to *Br. suis* or *Br. abortus*. From a worldwide point of view, *Br. melitensis* has induced a more serious economic and public health problem in animals and in man than has either of the other two varieties of Brucella. Of major concern in this country is the fact that *Br. melitensis* has become established in the swine population of Iowa and Minnesota, and human cases of *melitensis* disease have been attributed to contact with infected porcine material (5, 6). In the United States, at least, infection in cattle due to *Br. melitensis*

* James M. Anders Lecture XXIX, College of Physicians of Philadelphia, 1 April 1953.

From the Department of Medicine, University of Minnesota Hospitals and Medical School, Minneapolis, Minn.

is uncommon. The majority of the herds of goats in the United States are found west of the Mississippi in the western and southwestern states, and it is in these areas that foci of infected animals are present.

Although Bang (7) established the etiology of contagious abortion in cattle in 1897, it was not until 1918 that Evans (8) defined the antigenic relationship between *Br. melitensis* and *Br. abortus*, and emphasized the dangers to human health from cow's milk. A retrospective examination of the evidence indicates quite clearly that various individuals were correct in sounding warnings against Bang's disease as a cause of human disease, but the first undoubted human case of brucellosis due to *Br. abortus* was not reported until 1924 (9). By 1930, it was definitely established in the United States that Bang's disease in cattle constituted a real threat to human health, and the disease was contracted by either drinking raw milk or through contact of the abraded skin with infected animal tissues or body fluids. While the primary reservoir of *Br. abortus* is in cattle, this variant is also present in hogs in the United States (10). Investigations by Magoffin and his associates (11), and an unpublished survey carried out by the Committee on Public Health Aspects of Brucellosis of the National Research Council have shown that *Br. abortus* is responsible for the majority of cases of human brucellosis in the United States. In general, human brucellosis due to *Br. abortus* pursues a milder course than that caused by *Br. melitensis* or *Br. suis*.

Traum (12) first isolated *Br. suis* in 1914, and established this variant as the cause of contagious abortion in swine. Keefer (13) reported the first human case caused by *Br. suis* in 1924, which at that time was considered to be the first known case due to *Br. abortus*, but subsequent studies of the culture showed it to be *Br. suis* (14). The studies of Hardy and his group (15) reported from Iowa in 1930 further clarified the epidemiology of human brucellosis. The majority of their culturally proved cases were due to *Br. suis*, and they emphasized the association of the disease with certain occupations such as farming and working in meat packing plants. They concluded on the basis of epidemiologic and experimental studies that the abraded skin was an important site of entry for Brucella. While the natural reservoir of *Br. suis* is the hog, major epidemics of human brucellosis have been traced to cow's milk containing *Br. suis*, revealing that on occasion the tissues of cattle may be invaded by *Br. suis* (16, 17, 18). *Br. suis* causes a more severe infection in human beings than does *Br. abortus*, the course of the disease being characterized frequently by chronicity and suppuration.

There is no doubt that human beings become infected with Brucella through drinking contaminated milk, and through contact of the skin with infected tissues and body fluids of animals. There is additional experimental and clinical evidence that infection may occur through the respiratory tract and through the mucous membrane of the eye (19, 20).

Epidemiology of Human Brucellosis Due to Br. abortus

Although *Br. abortus* appears to be the cause of the majority of cases of human brucellosis in the United States, surprisingly scanty information is available on the epidemiology and clinical studies of a significant group of *bacteriologic-proved* cases. This paucity of information is due in large part to the failure of clinicians to employ proper cultural materials and techniques for the isolation of the organisms. In a previous study from this clinic, in cooperation with the Minnesota State Department of Health, epidemiologic data on a large group of culturally-proved cases were reported (11). The present report is not only concerned with the epidemiologic background, but also with follow-up clinical studies on a large number of patients studied in this clinic during the period 1937 through 1952. In these 15 years, hundreds of individuals have been examined for brucellosis, and the organisms have been isolated from 110 cases. This study demonstrates that even in an endemic area it takes a long time and persistent effort to ac-

cumulate a significant number of patients from whom precise bacteriologic data have been obtained. Of these 110 cases, 94 or 85.4%, were infected with *Br. abortus*, 11 with *Br. suis* and 5 with *Br. melitensis*. Quite clearly, the problem of brucellosis in our clinic is attributable to *Br. abortus*. In addition to these bacteriologic-proved cases, the diagnosis of active brucellosis has been made on 82 other patients from whom Brucella organisms were not isolated, but in whom the diagnosis was established upon the bases of epidemiologic, clinical and serologic evidence. Thus, the diagnosis of brucellosis was established in a total of 192 patients, which represents the definitive residue culled from hundreds of individuals with suspected brucellosis that were examined during these years.

For the present purposes, attention will be focused upon the 94 cases in which active disease was proved by the isolation of *Br. abortus* from their tissues or body fluids. From an epidemiologic viewpoint, an answer was desired for two questions. Who acquires this disease, and, how do they contract brucellosis? The answers were obtained and the data have been summarized in *Tables I and II*. In *Table I*, it is to be noted that of the 94 patients, 80 or 85% of the cases occurred in males. Furthermore, of the males, 60 or 75% of the cases were between the ages of 20 and 50 years. Another striking feature of the epidemiologic picture presented in *Table I* is that active brucellosis is uncommonly recognized in children. Turning now to *Table II* a partial answer was obtained as to why brucellosis is primarily a disease of males, and of males between 20 and 50 years of age. Of the 94 cases, 56 or 59.6% occurred in farmers or employees of meat packing plants. And if we include members of the farmers' families and veterinarians, the total number of cases is 70 or 74.5% of all the cases. This points out quite clearly that the majority of these cases of brucellosis occurred in individuals having *close contact* with livestock. Two points are emphasized with respect to employees in meat packing plants, and these are shown in *Table III*. First, 10 of the 27 persons having brucellosis due to *Br. abortus* had direct contact with only pork or pork products. This indicates that the porcine tissues were infected with *Br.*

TABLE I

Age and Sex Distribution of 94 Cases of Brucellosis (Br. abortus)

Age in years	No. of males	No. of females
0–4	2	0
5–9	1	0
10–14	2	1
15–19	6	0
20–29	26	3
30–39	24	3
40–49	10	1
50–59	5	4
60–69	4	2
Total	80	14

TABLE II

Occupation of 94 Cases of Brucellosis (Br. abortus)

Farmer	29	Laborer	1
Employee-Meat Packing Plant	27	Milk Collector	1
Farm Wife	6	Rancher	1
Farm Boy	4	Confectioner	1
Farm Girl	1	Highway Engineer	1
Veterinarians	3	Polisher and Buffer	1
House Wife	4	Interior Decorator	1
College Student	2	Furniture Buyer	1
School Boy	2	Hardware Store Clerk	1
School Girl	1	Radio Repair Work	1
Machinist	2	Sheet Metal Worker	1
Well Driller	1	Infant	1

TABLE III

Summary of Epidemiologic Data on Employees of Meat Packing Plants Having Brucellosis (Br. abortus)

Total Number of Cases		27
White Males	19	
Negro Males	6	
White Females	2	
No. of Cases Having Contact Only with Pork or Pork Products		10
No. Employed as Carpenters or Construction Workers		4

abortus, a fact which has been proved by McCullough, Eisele and Pavelchek (10). And second, there were 4 carpenters or construction workers, and 2 women who did not come in direct contact with animals or meat products. It is not known for certainty in what manner these individuals became infected, but it implies, at least, that the immediate environment of a plant must be heavily contaminated at times, and suggests the possibility of air-borne disease. And finally, significant epidemiologic data are presented in *Table IV* relative to farmers and their sources of infection. It is readily seen that the majority had ample reason for contracting the disease, since they came in contact with infected animals. Note that 10 of the 29 farmers handled aborted material from infected cows.

TABLE IV

SUMMARY OF EPIDEMIOLOGIC DATA ON FARMERS HAVING BRUCELLOSIS (BR. ABORTUS)

No. having positive reactors in herd of cattle	14
No. handling aborted material	10
No. in which source of infection undetermined	5
	29

There are one or two additional points relative to the epidemiology of brucellosis. While there is no question that human brucellosis can be contracted through the ingestion of unpasteurized milk or through the consumption of milk products, this aspect has been overemphasized since studies in Minnesota and elsewhere in the United States have shown that the disease for the majority of patients is acquired through direct contact with infected animals or their immediate environment (11, 21, 22). Another interesting aspect is that not a single laboratory worker is listed in the occupations of *Table II*. This indicates either that the laboratory personnel have been quite careful in their work or that *Br. abortus* is not highly invasive. Evidence has been accumulated over the years in our laboratory which reveals that carelessness will lead to an infection, but disease is more likely to occur after contact with the more invasive *suis* and *melitensis* strains. One laboratory worker contracted brucellosis due to *Br. suis*, and three others had positive cultures due to *Br. melitensis*.

The basic epidemiologic information to be gleaned from these studies on individuals with undoubted brucellosis, which should be of value to the clinician in his evaluation of suspected cases, is that brucellosis is primarily an occupational disease involving mostly males, who are in direct contact with infected animals, such as farmers and employees of meat packing plants. Less often, the disease is contracted through the ingestion of unpasteurized milk, and rarely an urban epidemic of brucellosis may be occasioned by milk (23). It is uncommon to recognize active brucellosis in children.

CLINICAL MANIFESTATIONS OF BRUCELLOSIS DUE TO BR. ABORTUS

The clinical data being presented are based upon studies of 94 cases having culturally-proved brucellosis due to *Br. abortus*. The *incubation period* of brucellosis is generally accepted to be anywhere from a week to 21 days. The present investigation indicates that this approximation holds true for the majority of cases. However, since brucellosis is for the most part an occupational disease in which multiple exposures to the disease take place, it is difficult to determine the precise time when infection did take place. Evidence has been obtained in some instances that a latent period of several months may intervene between the time of a single exposure to the disease, and the appearance of symptoms. In this respect brucellosis is like malaria in that many months may elapse between parasitization of the body and manifestations of the disease.

An analysis of 92 of the 94 cases showed that the *onset* of the illness was abrupt in 32 instances, and gradual in 60 patients.

Tabulation of the *symptomatology* is given in *Table V*. Patients with brucellosis have a

multiplicity of complaints, but the outstanding one in both the acutely and chronically ill patients is weakness. The principal group of complaints are those of weakness, chills, sweats, headache, and somatic aches and pains. Little surprise is then attached to the fact that the most commonly mistaken diagnosis was influenza. Brucellosis has a marked impact upon the nervous system as demonstrated by the frequency of the symptoms of nervousness, depression and insomnia. Because of this impact, a protracted illness in certain individuals may result in a residual of complaints long after active disease has subsided. Although 30 per cent of the patients complained of a cough, little evidence was accumulated relative to the infiltration of pulmonary parenchyma. Abdominal pain occurred in about one-fifth of the patients, and in three of these cases, surgical intervention was seriously considered. In general, the complaints referable to the gastro-intestinal tract were minor.

While patients with brucellosis may have a multitude of complaints, a minimum of abnormal findings are detected by physical examination, as seen in *Table VI*. In 92 out of 94 of the patients the presence of fever was demonstrated. In this clinic it has been very unusual to find a patient having active brucellosis without an elevated temperature. The descriptive type of undulating febrile reaction emphasized by Hughes (24) was lacking in these patients. The characteristic curve observed was a diurnal variation with the temperature down in the morning and elevated in the later afternoon or evening. In the more chronically ill patient considerable caution must be exercised in arriving at a diagnosis of brucellosis if the temperature is normal. That Brucella tend to localize in the reticulo-endothelial system is emphasized by enlargement of the lymph nodes and splenomegaly, which were demonstrated in almost one-half of the patients. Lymphadenopathy involved the anterior cervical, axillary and epitrochlear nodes. One-fourth of patients had enlarged livers, and in many instances the liver was tender to palpation, but jaundice was rare. The combination of fever, lymphadenopathy, splenomegaly and hepatomegaly often made the differential diagnosis between infectious mononucleosis and brucellosis difficult. The remaining physical abnormalities can be considered as complications of brucellosis.

TABLE V

SYMPTOMATOLOGY IN 94 CASES OF BRUCELLOSIS (BR. ABORTUS)

	NO. OF CASES	PER CENT OF CASES
Weakness	86	91.5
Sweats	72	76.5
Chills	71	75.5
Anorexia	66	70.0
Generalized aches	65	69.0
Headache	60	63.8
Rigors	52	56.3
Nervousness	49	52.0
Backache	48	51.0
Joint Pain	41	43.6
Depression	38	40.0
Insomnia	36	38.3
Pain back of neck	34	36.1
Cough	28	30.0
Abdominal pain	20	21.0
Constipation	11	11.6
Visual disturbances	11	11.6
Nausea and vomiting	9	9.6
Diarrhea	9	9.6
Genito-urinary disturbances	7	7.4
Neuralgia	5	5.3

TABLE VI

SIGNS IN 94 CASES OF BRUCELLOSIS (BR. ABORTUS)

	NO. OF CASES	PER CENT OF CASES
Fever	92	97.9
Lymphadenopathy	43	45.7
Palpable spleen	42	44.7
Palpable liver	24	25.5
Abdominal tenderness	8	8.5
Skin lesions	8	8.5
Neurologic changes	7	7.5
Cardiac abnormalities	7	7.5
Tenderness over spine	6	6.4
Funduscopic changes	3	3.2
Orchitis	2	2.1
Pain over hip joint	2	2.1
Jaundice	1	1.0
Pain over sacro-iliac joint	1	1.0

Complications of Brucellosis Due to Br. abortus

The most frequently encountered complication in the 94 cases was the involvement of bone, especially the spine, as noted in *Table VII*. Spondylitis with roentgenologic evidence of bone destruction occurred in the lumbar area in two patients, and in the thoracic and cervical regions in each of two other individuals. All of these patients recovered. Other bone lesions included a purulent arthritis of the hip joint and a destructive lesion of the sacroiliac joint. These two patients also recovered completely.

Subacute bacterial endocarditis occurred in four individuals, and three of these four patients had a fatal disease. The fourth patient had an aortic valvular lesion, and has remained well five years after receiving a combination of streptomycin and sulfadiazine. The detailed findings of two of the fatal cases have been presented elsewhere (25, 26). Brucella localized on normal valves in two of the patients, and on previously damaged valves of the two others. There were two other individuals among the 94 cases who had organic valvular lesions without evidence of active endocarditis, but who had a bacteremia. One patient had a mitral stenosis, and another had an aortic regurgitation associated with coarctation of the aorta. It is not unlikely that in these two patients prompt therapy with antibiotics prevented the establishment of a bacterial endocarditis.

TABLE VII

Complications in 94 Cases of Brucellosis (Br. abortus)

	No. of cases
Spondylitis	4
Destructive lesion sacro-iliac joint	1
Purulent arthritis hip joint	1
Subacute bacterial endocarditis	4
Chronic meningitis	2
Orchitis	2
Cholecystitis	2
Neuritis	2
Mesenteric adenitis	1
Cirrhosis of the liver	1

There were two patients with chronic meningitis of two and four years' duration from whose cerebrospinal fluid *Br. abortus* was isolated. The details of illness of these patients have been recorded elsewhere (27). Both individuals recovered after therapy with aureomycin. Two individuals had orchitis. This complication is less frequently encountered, apparently, in infections due to *Br. abortus* than those due to *Br. melitensis*. Two individuals with an associated acute cholecystitis, one with jaundice, recovered without surgical intervention. Two individuals had a severe peripheral neuritis, and again, it would appear that this complication occurs more frequently in disease caused by *Br. melitensis*. One individual with a mesenteric adenitis had abdominal pain which simulated that of acute appendicitis, and surgical intervention was seriously considered. As has been pointed out (28), hepatitis can be frequently demonstrated in patients with brucellosis by biopsy of the liver. Most clinicians who have studied brucellosis extensively believe that brucellosis may be one of several factors which may cause cirrhosis of the liver in an occasional patient. In the present series, serial biopsy studies indicated that cirrhosis of the liver was induced by *Br. abortus* in one patient.

The Use of Laboratory Procedures in the Diagnosis of Brucellosis

Although the clinician may suspect the diagnosis of brucellosis on the basis of epidemiologic information, a precise diagnosis is dependent upon laboratory data (29, 30). An unequivocal diagnosis is established when Brucella organisms are isolated from the body fluids or tissues of suspected cases. In the present series of 94 cases due to *Br. abortus*, the organisms were isolated from venous cultures of blood in 88 of the patients. Although blood cultures remained sterile in 6 of the patients, *Br. abortus* was isolated from aspirated sternal bone marrow in 3, the cerebrospinal fluid in 2, and from exudate obtained

from the hip joint in 1. Our experience has led us to conclude that the most desirable cultural media for Brucella are "Trypticase-soy" broth or "Albimi" Brucella medium. Tryptose broth is a satisfactory, though less efficient medium. The double-media of Castaneda is employed in which broth is added to a rectangular bottle and agar is then dispersed along one side of the container (31).

The next most helpful diagnostic aid is the agglutination test. With the widespread, and often indiscriminate, use of antibiotics for undefined febrile disturbances, the agglutination test will assume more and more importance in the diagnosis of brucellosis. Unfortunately, much confusion and misunderstanding has been associated with the significance and interpretation of the agglutination reaction. This has been due in large part to the use of unreliable antigens and to the employment of unstandardized techniques. In our clinic the same antigen has been used for several years with the tube-dilution technique. The antigen is derived from a strain of *Br. abortus*, and has been supplied by the Bureau of Animal Industry of the United States Department of Agriculture. The results in the University of Minnesota Hospitals, as well as in the Laboratories of the Minnesota State Department of Health, have shown that it is extremely rare to isolate *Br. abortus* from blood in which Brucella agglutinins are absent. Over a period of 15 years, as seen in *Table VIII*, only one patient had a positive blood culture with no demonstrable agglutinins. In this particular case, Hall and Manion (32) demonstrated a high titer of blocking antibodies in the serum of this patient. It must be added, that except in a rare case, blocking antibodies are of little practical significance in the diagnostic application of the agglutination test. This also applies to the prozone phenomenon. Another feature of our experience with the agglutination test is that over 90 per cent of the cases had titers of 1 to 320 or above. It must be emphasized that in an endemic area of brucellosis, a significant segment of the normal population will have low titers of agglutinins (33). Unless accompanied by other definitive evidence we interpret titers of less than 1 to 160 with some doubt as far as active brucellosis is concerned. Patients suffering from the residuals of brucellosis may have a low titer of agglutinins extending over a period of several years (34).

As in any febrile disease of doubtful etiology the attention of the clinician is attracted to the results of the total and differential leukocyte counts in the peripheral blood. In brucellosis, this information may be of distinct value. As seen in *Table IX*, patients having brucellosis with a demonstrable bacteremia have either a normal total leukocyte count or a tendency toward a leukopenia. Only 7 patients had values above 10,000 on the same day that *Br. abortus* was isolated. Another feature of the peripheral blood is the presence of a relative lymphocytosis. Over 50 per cent of the patients had differential counts with more than 40

TABLE VIII

Reciprocal of Agglutinin Titer in 94 Cases of Brucellosis (Br. abortus)

TITER	NO. OF CASES
0	1
80	0
160	6
320	13
640	25
1280	22
2560	17
5120	10

TABLE IX

Total Leukocyte Count of 93 Cases of Brucellosis (Br. abortus)

TOTAL LEUKOCYTES PER CU. MML.	NO. OF CASES
2000–2900	2
3000–3900	11
4000–4900	10
5000–5900	24
6000–6900	19
7000–7900	10
8000–8900	3
9000–10000	7
Above 10000	7

per cent lymphocytes. It was not unusual to encounter blood films having an abundance of leukocytoid forms of lymphocytes such as is encountered in infectious mononucleosis. The similarities of the clinical and hematologic pictures of infectious mononucleosis and brucellosis make the distinction difficult at times (35).

While the erythrocyte sedimentation rate is uniformly accelerated in most bacterial infections, it was observed in this and in a previous study that the sedimentation rates of bacteremic patients with and without complications may be normal or accelerated (*Table X*) (36). Although this laboratory procedure is without diagnostic value, it is of some prognostic aid in the treatment of these patients.

TABLE X

Erythrocyte Sedimentation Rate (Westergren) in 93 Cases of Brucellosis (Br. abortus)

MMS. PER HOUR	NO. OF CASES
0–4	5
5–9	6
10–19	17
20–29	18
30–39	10
40–49	10
50–59	7
60–69	4
70–79	7
80–89	4
90–100	4

Since the results of the complement-fixation test paralleled those of the agglutination reaction, the former procedure was abandoned several years ago in our clinic for diagnostic purposes. We also concluded after a reasonable period of investigation that the opsonocytophagic test was of very questionable value as a diagnostic aid, particularly in the sporadic and doubtful case of brucellosis. In no instance, did the results of this test aid in the differential diagnosis. At present, it is strictly a research tool.

The intradermal test employing Brucella antigen is not properly a laboratory procedure, but since it is used widely for diagnostic purposes, our evaluation of this test should be mentioned. After comparative studies with a number of different antigens, the intradermal test for diagnostic purposes has been given up completely (37). It was observed that up to 20 per cent of adults living in rural, endemic areas of brucellosis had positive dermal reactions (38). Furthermore, the presence of a positive skin test in a doubtful case often provoked more confusion than enlightenment. The intradermal test is employed only for epidemiologic purposes, which is in agreement with the recommendation of the National Research Council, and with the conclusions of the Expert Committee on Brucellosis of the World Health Organization and Food and Agricultural Organization (30, 39).

The Treatment of Human Brucellosis

One of the major pursuits of my associates and myself since we initiated our investigations on brucellosis has been an evaluation of therapy. Utilizing *in vitro* screening methods, as well as the treatment of experimentally infected chick embryos, mice, guinea pigs and rabbits, many therapeutic agents have been investigated. Promising therapeutic leads obtained in this way have then been applied to the treatment of human patients. Before summarizing the results of these efforts, it is well to refer to the natural course of brucellosis. Comparative clinical observations made in our clinic and in other clinics in various parts of the world have revealed that, in general, brucellosis due to *Br. abortus* causes a relatively mild and uncomplicated disease when compared to illness due to *Br. melitensis* or *Br. suis*. As a consequence, the majority of patients having an infection due to *Br. abortus* recover completely from their illness with the passage of time, and usually within 6 to 12 months. This is also true to a lesser extent for patients with infections due to *Br. melitensis* or *Br. suis*. In many respects, brucellosis is like malaria. Very often, febrile patients will obtain relief from their symptoms and achieve recovery within a relatively brief period of time follow-

ing rest in bed. This feature of brucellosis must be borne in mind when attempting to evaluate any therapeutic agent or agents in brucellosis.

The evaluation in drug therapy for brucellosis has followed the introduction of the sulfonamides and antibiotics which have been introduced into medicine since 1937, when sulfanilamide first became available. This is reflected in the therapy which the 94 patients with brucellosis due to *Br. abortus* received as shown in *Table XI*.

Early *in vitro* experiments showed that the sulfonamides inhibited the multiplication of Brucella cells, but the cultures were not sterilized. A significant number of patients were then treated and the final results are presented in *Table XII*. Coincident with the use of sulfanilamide, sulfapyridine, sulfathiazole, sulfadiazine or sulfamerazine, slightly more than 50 per cent of 20 patients progressively recovered. The sulfonamides had no favorable effect upon the lethal course of subacute bacterial endocarditis, and bacteriologic and clinical relapses were encountered. It could only be concluded that at best the sulfonamides were suppressive agents for brucellosis, and that they were not the definitive answer to therapy. When penicillin became available it was readily observed that this antibiotic was without demonstrable effect on the course of bacteremic brucellosis. Experimental and clinical investigations with streptomycin provided us with paradoxical results. It was demonstrated *in vitro* that streptomycin had a marked bactericidal action on Brucella, rapidly killing large numbers of organisms (40, 41). Furthermore, the antibiotic offered protection to experimentally infected chick embryos (42, 43). But when streptomycin was administered to human patients, there was little beneficial effect noted on the clinical course. A probable explanation for this therapeutic paradox was not to be forthcoming until later, and will be referred to shortly. Exploratory experiments had pointed to the possible superiority of two agents administered simultaneously, and it was concluded that a combination of streptomycin and sulfadiazine had a synergistic action against Brucella (44). When such a combination was administered to patients, the results were as anticipated (45, 46). A more satisfactory approach to brucellosis appeared to be at hand, and our results supported that of others (47, 48). Most remarkable in our own results was the recovery of patients with serious complications. For the first time a patient with subacute bacterial endocarditis due to *Br. abortus* was treated successfully at the University Hospitals. In spite of this initial enthusiasm when the final results were brought together, as is seen in *Table XIII*,

TABLE XI

TREATMENT IN 94 CASES OF BRUCELLOSIS (BR. ABORTUS)

Total with no treatment	4
Total receiving sulfonamides	20
Total receiving penicillin	3
Total receiving streptomycin	6
Total receiving streptomycin and sulfadiazine	22
Total receiving aureomycin	25
Total receiving chloramphenicol	7
Total receiving streptomycin and aureomycin	5
Total receiving adrenocorticotrophic hormone	2

TABLE XII

THE RESULTS OF TREATMENT WITH SULFONAMIDES IN 20 PATIENTS WITH BRUCELLOSIS (BR. ABORTUS)

No. of cases—progressive recovery	11
No. of deaths—(subacute bacterial endocarditis)	2
No. of cases—bacteriologic relapse	4
No. of cases—clinical relapse	1
No. of cases—doubtful or no benefit	2

TABLE XIII

THE RESULTS OF TREATMENT WITH STREPTOMYCIN AND SULFADIAZINE IN 22 PATIENTS WITH BRUCELLOSIS (BR. ABORTUS)

No. of cases—progressive recovery	12
No. of cases—gradual recovery	3
No. of cases—bacteriologic relapse	5
No. of cases—clinical relapse	2

there was still a significant group of patients who did not respond as favorably as desired. More recently, investigations have been carried out with aureomycin. Although *in vitro* studies by Yow and Spink (41) had shown that aureomycin was a bacteriostatic, and not a bactericidal agent for Brucella, and investigations with the infected chick embryo and experimentally infected mice had demonstrated that aureomycin acted as a suppressive drug and it did not eradicate the organisms from the tissues, when aureomycin was administered orally to patients with infections due to *Br. abortus* or to *Br. melitensis*, the therapeutic results were better than had been anticipated (49, 50, 51, 52). The over-all results with aureomycin are presented in *Table XIV*. The results with aureomycin

TABLE XIV

THE RESULTS OF TREATMENT WITH AUREOMYCIN IN 17 PATIENTS WITH BRUCELLOSIS (BR. ABORTUS)

No. of cases—progressive recovery	17
No. of cases—gradual recovery	2
No. of cases—bacteriologic relapse	3
No. of cases—clinical relapse	2
No. of cases—failure because toxic effect of drug	1

have been more favorable than those obtained with streptomycin and sulfadiazine, and those with chloramphenicol.

An investigation of the host-parasite relationship in chronically infected animals with respect to treatment has emphasized certain aspects of the mechanism of recovery and eradication of Brucella from the tissues (53). It was concluded that the eventual elimination of the bacteria depended upon the combined action of the defense mechanism of the host and therapeutic agents. The drugs, acting as suppressive agents, abetted the immune mechanism of the host, and optimum results were obtained in those animals given prolonged treatment with a combination of drugs, such as streptomycin plus sulfadiazine, aureomycin, or terramycin, rather than treatment with any one of these drugs used alone.

A follow-up study of patients treated with antibiotics has indicated quite clearly that definite advances have been made in the therapy of brucellosis (54). However, there still remains a significant group of patients, who even after receiving what is considered to be adequate treatment, do have clinical and bacteriologic relapses. Complete eradication of Brucella organisms does not apparently take place in some patients because of the intracellular localization of the bacteria (55). Experimental observations have shown that the organisms inside of cells are protected against the lethal action of chemotherapeutic agents and immune serum (56, 57). In an attempt to dislodge the Brucella organisms from their intracellular position, cortisone was administered to experimentally infected animals (58). The results were disastrous for the acutely infected animals, and without apparent effect upon those chronically infected. When adrenocorticotrophic hormone (ACTH) was given to human patients with bacteremia there was a dramatic improvement in their condition, although the bacteremia persisted (59). It is recommended that for the seriously ill and toxic patient with brucellosis, ACTH or cortisone should be administered for 24 to 48 hours simultaneously with a combination of streptomycin or dihydrostreptomycin and aureomycin or terramycin. The antibiotics should be given for a minimum of two weeks.

PREVENTION OF BRUCELLOSIS

The elimination of brucellosis as a human disease is solely dependent upon the eradication of the disease in domestic animals. In the United States the major reservoir is in dairy and beef cattle, although swine brucellosis is also of serious concern. Leaders in the effort to control brucellosis have adopted the philosophy of complete eradication of the disease rather than living with the disease. Methods that have been employed in animals include the testing, immunizing and slaughtering of herds. Progress has not been made without considerable work and controversy. The fear of economic suicide, misunderstanding, and

ignorance have often thwarted well designed plans. But through the coordinated efforts of livestock groups, the dairy industry, veterinarians, public health authorities, and physicians, great strides have been made since World War II in eliminating animal brucellosis. When this has been accomplished human brucellosis will cease as a problem of public health.

BIBLIOGRAPHY

1. Bruce, D.: Note on the discovery of a microorganism in Malta Fever, Practitioner, **39:** 161, 1887.
2. Reports of the Commission appointed by the Admiralty, the War Office, and the Civil Government of Malta, for the Investigation of Mediterranean Fever, under the supervision of an Advisory Committee of the Royal Society, Parts I–VII, London, Harrison & Sons, 1905–1907.
3. Cantaloube, P.: La Fièvre de Malta en France, Maloine, Paris, 1911.
4. Braude, A. I.: Studies in the pathology and pathogenesis of experimental brucellosis. I. A comparison of the pathogenicity of Brucella abortus, Brucella melitensis, and Brucella suis for guinea pigs, J. Infect. Dis., **89:** 76, 1951.
5. Jordan, C. F., and Borts, I. H.: Occurrence of Brucella melitensis in Iowa, J.A.M.A., **130:** 72, 1946.
6. Kabler, P., Bauer, H., and Nelson, C. B.: Human Brucella melitensis infections in Minnesota with hogs as the probable source, J. Lab. & Clin. Med., **32:** 854, 1947.
7. Bang, B.: Die aetiologie des seuchenhaften ("infectiösen") Verwerfens. Ztschr. Tiermed., **1:** 241, 1897.
8. Evans, A. C.: Further studies on Bacterium abortus and related bacteria II. J. Infect. Dis., **22:** 580, 1918.
9. Orpen, L. J.: The connection between undulant (Malta) fever and contagious abortion, Tr. Roy. Soc. Trop. Med. Hyg., **17:** 521, 1924.
10. McCullough, N. B., Eisele, C. W., and Pavelchek, E.: Isolation of Brucella abortus from hogs, Public Health Reports, **64:** 537, 1949.
11. Magoffin, R. L., Kabler, P., Spink, W. W., and Fleming, D.: An epidemiologic study of brucellosis in Minnesota, Pub. Health Rep., **64:** 1021, 1949.
12. Traum, J.: Infectious abortion investigations in pigs, Annual Report, U. S. Dept. of Agriculture, P. 86, 1914.
13. Keefer, C. S.: Report of a case of Malta fever originating in Baltimore, Md., Johns Hopkins Hosp. Bull., **35:** 6, 1924.
14. Huddleson, I. F.: Brucellosis in man and animals, P. 56, New York, Commonwealth Fund, 1939.
15. Hardy, A. V., Jordan, C. F., Borts, I. H., and Hardy, G. C.: Undulant fever with special reference to a study of Brucella infection in Iowa. Nat. Inst. Health Bull., 158, 1930.
16. Beattie, C. P., and Rice, R. M.: Undulant fever due to Brucella of the porcine type—Brucella suis. Report of a milk-borne epidemic, J.A.M.A., **102:** 1670, 1934.
17. Horning, B. G.: Outbreak of undulant fever due to Brucella suis, J.A.M.A., **105:** 1978, 1935.
18. Borts, I. H., Harris, D. M., Joynt, M. F., Jennings, J. R., and Jordan, C. F.: A milk-borne epidemic of brucellosis caused by the porcine type of Brucella (Brucella suis) in a raw milk supply, J.A.M.A., **121:** 319, 1943.
19. Molinelli, E. A., Fernandez-Ithurrat, E. M., and Ithurralde, D.: Epidemiologia de la brucelosis humana en la Republica Argentina, Rev. Asoc. Méd. Argent., **62:** 111, 1948.
20. Elberg, S. S., and Henderson, D. W.: Respiratory pathogenicity of Brucella, J. Infect. Dis. **82:** 302, 1948.
21. Jordan, C. F., and Borts, I. H.: Brucellosis and infection caused by three species of Brucella, Am. J. Med., **2:** 156, 1947.
22. Zintek, A. R.: Brucellosis in Wisconsin, Wisconsin M. J., **49:** 205, 1950.
23. Steele, J. H., and Hastings, J. W., Sr.: Report of brucellosis outbreak at Federalsburg, Maryland, Pub. Health Rep., **63:** 144, 1948.
24. Hughes, M. L.: Mediterranean, Malta or Undulant Fever, London, Macmillan, 1897.
25. Spink, W. W., and Nelson, A. A.: Brucella endocarditis, Ann. Int. Med., **13:** 721, 1939.
26. Spink, W. W., Titrud, L. A., and Kabler, P.: A case of Brucella endocarditis with clinical, bacteriologic and pathologic findings, Am. J. Med. Sci., **203:** 797, 1942.
27. Spink, W. W., and Hall, W. H.: Encephalomeningitis due to Brucella abortus, Tr. Am. Clin. Climatol. A., **61:** 121, 1949.
28. Spink, W. W., Hoffbauer, F. W., Walker, W. W., and Green, R. A.: Histopathology of the liver in human brucellosis, J. Lab. & Clin. Med., **34:** 40, 1949.
29. Spink, W. W.: The laboratory in the diagnosis of brucellosis, Am. J. Clin. Path., **22:** 201, 1952.
30. Spink, W. W., McCullough, N. B., Hutchings, L. M., and Mingle, C. K.: Diagnostic criteria for human brucellosis: Report No. 2 of the National Research Council, Committee on Public Health Aspects of Brucellosis, J.A.M.A., **149:** 805, 1952.
31. Castaneda, M. R.: A practical method for routine blood cultures in brucellosis, Proc. Soc. Exper. Biol. & Med., **64:** 114, 1947.

32. Hall, W. H., and Manion, R. E.: Comparison of the Coombs test with other methods for Brucella agglutinins in human serum, J. Clin. Investigation, **32:** 96, 1953.
33. Spink, W. W., and Anderson, D.: Brucella studies on bank blood in a general hospital, J. Lab. & Clin. Med., **35:** 440, 1950.
34. Spink, W. W.: What is chronic brucellosis? Ann. Int. Med., **35:** 358, 1951.
35. Spink, W. W., and Anderson, D.: Studies relating to the differential diagnosis of brucellosis and infectious mononucleosis: clinical, hematologic and serologic observations, Tr. A. Am. Physicians, **64:** 428, 1951.
36. Agnew, S., and Spink, W. W.: The erythrocyte sedimentation rate in brucellosis, Am. J. M. Sci., **217:** 211, 1949.
37. Braude, A. I.: Dermal hypersensitivity in human brucellosis, Staff Meet. Bull. Hosp. Univ. of Minn., **19:** 254, 1948.
38. Spink, W. W., Hall, W. H., and Aagaard, G. N.: Chronic brucellosis, Staff Meet. Bull. Hosp. Univ. of Minn., **17:** 194, 1946.
39. Report of Joint FAO and WHO Expert Committee on Brucellosis, Second Session, Florence, Italy Oct. 13–18, 1952.
40. Hall, W. H., and Spink, W. W.: *In vitro* sensitivity of Brucella to streptomycin: development of resistance during streptomycin treatment, Proc. Soc. Exper. Biol. & Med., **64:** 403, 1947.
41. Yow, E. M., and Spink, W. W.: Experimental studies on the action of streptomycin, aureomycin and chloromycetin on Brucella, J. Clin. Investigation, **28:** 871, 1949.
42. Hall, W. H., and Spink, W. W.: Therapy of experimental Brucella infection in the developing chick embryo, I. Infection and therapy via the allantoic sac, J. Immunol., **59:** 379, 1948.
43. Shaffer, J. M., and Spink, W. W.: Therapy of experimental Brucella infection in the developing chick embryo, II. Infection and therapy via the yolk sac, J. Immunol., **59:** 393, 1948.
44. Shaffer, J. M., and Spink, W. W.: Therapy of experimental Brucella infection in the developing chick embryo, III. The synergistic action of streptomycin and sulfadiazine, J. Immunol., **60:** 405, 1948.
45. Spink, W. W., Hall, W. H., Shaffer, M. J., and Braude, A. I.: Human brucellosis: Its specific treatment with a combination of streptomycin and sulfadiazine, J.A.M.A., **136:** 382, 1948.
46. Spink, W. W., Hall, W. H., Shaffer, J., and Braude, A. I.: Treatment of brucellosis with streptomycin and a sulfonamide drug. J.A.M.A., **139:** 352, 1949.
47. Pulaski, E. J., and Amspacher, W. H.: Streptomycin therapy in brucellosis, Bull. U. S. Army M. Dept., **7:** 221, 1947.
48. Eisele, C. W., and McCullough, N. B.: Combined streptomycin and sulfadiazine treatment in brucellosis, J.A.M.A., **135:** 1053, 1947.
49. Magoffin, R., Anderson, D., and Spink, W. W.: Therapy of experimental Brucella infection in the developing chick embryo, IV. Therapy with aureomycin, J. Immunol., **62:** 125, 1949.
50. Braude, A. I., and Spink, W. W.: The action of aureomycin and other chemotherapeutic agents in experimental brucellosis, J. Immunol., **65:** 185, 1950.
51. Spink, W. W., Braude, A. I., Castaneda, M. R., and Silva-Goytia, R.: Aureomycin therapy in human brucellosis due to Brucella melitensis, J.A.M.A., **138:** 1145, 1948.
52. Braude, A. I., Hall, W. H., and Spink, W. W.: Aureomycin therapy in human brucellosis due to Brucella abortus, J.A.M.A., **141:** 831, 1949.
53. Shaffer, J. M., Kucera, C. J., and Spink, W. W.: Evaluation of prolonged antibiotic therapy in mice with chronic Brucella infection due to Brucella melitensis, J. Immunol., **70:** 31, 9153.
54. Spink, W. W., Hall, W. H., and Magoffin, R.: Follow-up study of therapy in forty-eight culturally proved cases of brucellosis, Arch. Int. Med., **88:** 419, 1951.
55. Spink, W. W.: Some biologic and clinical problems related to intracellular parasitism in brucellosis, New England J. Med., **247:** 603, 1952.
56. Magoffin, R. L., and Spink, W. W.: The protection of intracellular Brucella against streptomycin alone and in combination with other antibiotics, J. Lab. & Clin. Med., **37:** 924, 1951.
57. Shaffer, J. M., Kucera, C. J., and Spink, W. W.: The protection of intracellular Brucella against therapeutic agents and the bactericidal action of serum, J. Exper. Med., **97:** 77, 1953.
58. Abernathy, R., and Spink, W. W.: The influence of cortisone and adrenocorticotrophic hormone on brucellosis, I. Cortisone in experimentally infected animals, J. Clin. Investigation, **31:** 947, 1952.
59. Spink, W. W., and Hall, W. H.: The influence of cortisone and adrenocorticotrophic hormone on brucellosis, II. Adrenocorticotrophic hormone (ACTH) in acute and chronic human brucellosis. J. Clin. Investigation, **31:** 958, 1952.

The Vanishing Spas of Pennsylvania (An Historical Review)*

By IGHO H. KORNBLUEH†, M.D., AND GEO. MORRIS PIERSOL‡, M.D.

Part I

THE majority of American people today admittedly are indifferent to the therapeutic value of spas. For the most part, the physicians of this country also lack interest in this type of treatment. That such an attitude towards spa therapy was not held by our ancestors may be inferred from the numerous watering places that flourished during the colonial days and throughout the first century of this Republic's history. Many of these establishments were extensively patronized and enjoyed great popularity, as well as the approval and support of the contemporary medical profession.

The early white settlers of the State of Pennsylvania came chiefly from European countries, in which therapeutic baths and mineral springs had been in vogue for 2000 years. These people had learned to supplement the deficiencies of the medical practice of their day by what has been termed "natural treatments." It is not surprising, therefore, that when individuals with such a background found themselves in a vast virgin territory of untold natural resources and an abundance of water, they should have developed in their new surroundings facilities for spa therapy in which by tradition and training they had faith. The State of Pennsylvania lent itself well to such therapeutic purposes because of its geological formation. Throughout the State, many springs and wells were to be found, the waters of which vary in temperature and contain significant amounts of one or several chemicals such as iron, magnesia, sulfur, and hydrogen sulfide. Such natural resources placed for the most part in an attractive setting afforded exceptional opportunity to establish spas. As a consequence, at various times during the past 200 years, at least 30 such institutions are known to have existed in this State. In addition, over 50 so-called mineral springs not combined with buildings for the housing of guests and patients have been recorded.

Up until the middle of the last century health resorts and therapeutic springs in the Eastern United States attained considerable popularity and success. From that time down to the present interest in spa therapy throughout this country has steadily declined. In this respect, Pennsylvania's experience has not differed from that observed elsewhere throughout the United States. Of the 30 spas that were developed in Pennsylvania at different places and at various periods only three are presently active. The remaining 27 have been abandoned, destroyed by fire or otherwise, or have been converted to different uses. It is a significant commentary on the thinking of the times that efforts were never made to restore these watering places or to establish others at new locations. The several causes responsible for the gradual decline of the North American spas over the last 75 years have been discussed by Sigerist (1, 2) in his admirable historical reviews. The factors underlying the disappearance of health resorts from Pennsylvania have been analyzed by Kornblueh and Piersol (3). It was pointed out that in the case of that State, as elsewhere, the most important factor has been the revolutionary changes that have occurred in medical practice during the last half century which have led to professional

* Read in part before the College of Physicians of Philadelphia, Section on Medical History, 29 January 1953.

† Instructor in Physical Medicine, Graduate School of Medicine, University of Pennsylvania, Philadelphia.

‡ Professor of Medicine, Chairman, Department of Physical Medicine and Rehabilitation, Graduate School of Medicine, University of Pennsylvania, Philadelphia.

apathy towards balneo- and climato-therapy. However, other influences have played significant roles in elimination of spas. The widespread industrialization of the State, the development of farming, mining, the rapid growth of towns and cities, the extension of railways and new highways, often located inconveniently far from existing resorts, have contributed to the situation. Serious responsibility for the plight of the health resorts rests upon some of the owners and managers, who not only have been guilty of exaggerated advertising and ill-considered exploitation of their facilities and mineral waters, but have failed to modernize their institutions in such a way as to appeal to a critical public. Thus far, the few sporadic attempts of enthusiastic investigators to revive interest in spa therapy have been conspicuously unsuccessful in overcoming the growing apathy towards health resorts that is so apparent among the laity and physicians of this country.

The subjects of balneology and hydrotherapy were looked upon with much interest by the early physicians of Pennsylvania. In 1767, Adam Kuhn (4), a native of Pennsylvania, discussed the value of cold baths in his dissertation for the degree of Doctor of Medicine at the University of Edinburgh. The value of Kuhn's treatise, "De Lavatione Frigida," was recognized by his contemporary, Benjamin Rush (5), in the latter's directions for use of the water at Harrowgate near Philadelphia. "It (cold bath) not only cures these diseases," wrote Rush, "but frequently removes barrenness and prevents abortion." Bell added two valuable contributions on baths and the use of mineral waters (6, 7).

It is interesting that, years later, Guy Hinsdale (8), also of Philadelphia, wrote a comprehensive work on hydro- and balneotherapy, which may be regarded as the most complete and advanced contribution to that subject up to that time. Its value and significance is enhanced by an appendix dealing with truths about hydrotherapy contributed by Simon Baruch.

H. W. Lockett (9) became an enthusiastic champion of warm baths. In his thesis, on the merits of the warm bath, Lockett stressed the value of warm water in old age. He mentioned Dr. Franklin, who was helped by such treatments. "It prevented the too rapid approach of old age, and enabled him to support the infirmities of his last days with less perceptable decay." Lockett thought that warm baths must be taken regularly and for long periods of time, to obtain the desirable therapeutic effects. Contrary to the views of his teacher, Rush, Lockett was not impressed by the therapeutic value of mineralized water. "I do not believe there is that difference between the medicated and simple baths as has been hitherto supposed; and that their success depends more on the change of climate, exercise, and perseverance, than on any peculiar property possessed by the waters."

This review is not intended as a requiem for the vanishing spas of Pennsylvania. It was undertaken to show that during their ascendency watering places occupied a significant place in the social life of that State and that they were closely associated with many events of political and historical importance. Furthermore, to emphasize that they were accorded serious consideration by the physicians and citizens of that day and had a definite influence upon medical thought and therapeutic practice.

It became apparent that the material for this contribution could be collected satisfactorily only by a personal inspection. Therefore, the senior author embarked upon a series of field surveys conducted during 1951 and 1952, and the early spring of 1953. All the existing watering places and known mineral springs in Pennsylvania, as well as the sites of former establishments, were visited by him. During these investigations, which involved thousands of miles of travel, many difficulties were encountered and endless patience exercised. The success attained was made possible, in large measure, through the cooperation of many professional and lay

TABLE 1

SPAS NO LONGER IN EXISTENCE

NO.	NAME	COUNTY
1	Blossburg	Tioga
2	Bristol Bath Springs	Bucks
3	Caledonia Springs (or Sweeney's Cold Springs)	Adams
4	Carlisle Springs	Cumberland
5	Chester (Yellow) Springs	Chester
6	Cresson	Cambria
7	Doubling Gap	Cumberland
8	Ephrata	Lancaster
9	Fayette Springs	Fayette
10	Frankfort Mineral Springs	Beaver
11	Gardeau	McKean
12	Gettysburg	Adams
13	Graeffenburg	Adams and Franklin
14	Pavillon Spring, Wernersville	Berks
15	Huntingdon	Huntingdon
16	Kiskiminetas	Indiana
17	Loganton	Clinton
18	Minnequa Springs	Bradford
19	Monterey	Franklin
20	Mt. Holly	Cumberland
21	Perry Warm Springs	Perry
22	Pulaski	Lawrence
23	Saegerstown	Crawford
24	Sizerville	Cameron
25	Three Springs	Huntingdon
26	Tuckhoe Mineral Springs	Northumberland
27	York Springs	Adams

TABLE 2

PLACES WHERE FORMER HOTELS ARE STILL PRESERVED AND THEIR PRESENT STATUS

NO.	NAME	USED RECENTLY AS
1	Bedford Chalybeate Hotel	Residence
2	Chester (Yellow) Springs	Closed
3	Doubling Gap	Church and Retreat
4	Ephrata	Closed
5	Graeffenburg	Resort
6	Grand View Sanatorium (Pavillon Spring)	Apartment House
7	Kiskiminetas	Prep School
8	Mt. Holly	Residence
9	Perry Warm Springs	Residence
10	Tuckhoe Mineral Springs	Residence

residents of various localities[1]. To all of them we express thanks for their unfailing cooperation and guidance. The location and names of former Pennsylvania spas were obtained from old medical literature, periodicals, newspapers, and county histories.

By the middle of 1953, over 50 mineral springs and 30 spas or their former sites had been visited. In the tables the names of the spas are recorded in alphabetical order, rather than according to geographical location.

In general, during the following detailed discussion of Pennsylvania's spas, alphabetical arrangement is followed. An exception has been made in the case of the spas in and around Philadelphia. For the sake of convenience they are considered below as a group.

The spas in the vicinity of Philadelphia achieved fame not only because of their proximity to and close association with the history of that city, but also through their medical activities.

TABLE 3

PRESENTLY ACTIVE SPAS

NO.	NAME	COUNTY
1	Bedford Springs	Bedford
2	Cambridge Springs	Crawford
3	White Sulphur Springs	Bedford

Philadelphia Area

One of the best known of the group, situated in Bucks County near Bristol was Bath Springs, noted for its chalybeate waters. When

[1] We are especially indebted to the Secretary of Health of the Commonwealth of Pennsylvania, Dr. Russell E. Teague, for his generous collaboration and for making available the technical help and assistance of members of his staff, including the several District Engineers. This staff includes: Mr. H. E. Moses, Consulting Chief Engineer, Mr. J. R. Hoffert, Chief Engineer, Mr. L. D. Matter, Assistant Chief Engineer, and the District Engineers, Messers, B. S. Bush, E. Edgerley, J. R. Harvey, R. W. Kremer, L. K. Scheffer, and M. E. Wilt. We are especially grateful for the constant advice and assistance of Mr. George A. Elias, who did so much to make the survey possible.

founded about 1697, Bristol was called Buckingham (10). Twenty-three years later, the name was changed to Bristol. Bristol developed relatively early many hostelries and became a favorite stopover on the stagecoach runs from Philadelphia to Trenton and for the river boats. The water of the chalybeate springs, located a short distance from the town was known to the early settlers of this region but attained little popularity. Green (11) states that the colonists referred to this water as the "nasty water". It was certainly not a pure iron water, as its name implies. It had the taste and smell of slightly rotten eggs, indicating its hydrogen sulphide content. At a time when assimilable iron components were unknown an iron spring was a welcome asset to the many suffering from iron deficiency anemias, common because of the prevalence of nutritional disorders. The generally sun-shy city dwellers, especially the women, made good use of this spa as a source of iron, sunshine, baths, and perhaps also for a touch of personal liberty. The renowned chalybeate water was used in its natural state for gargling, foot baths, and drinking, while general hot baths were available in the bath house. The psychosomatic methods as applied in Bath Springs were here in good and experienced hands.

Entertainment and horse races offered the needed diversion to the great multitude of guests and visitors. This pleasing aspect of life in Bath Springs was considerably offset by the "number of idle and disorderly persons, who constantly resort there, especially on the first day of the week, usually called Sunday." The fathers of the borough decreed, therefore, at a meeting of August 7, 1769, "Every person (here follow a few exceptions) that shall be found loitering about or within the limits of said bath shall . . . be taken into custody unless they disperse. . . ."

Bache's history of Bristol Borough mentions that the Springs were already widely known in 1722, while 47 years later the Borough recorded wells at Bristol Bath. Both statements, made

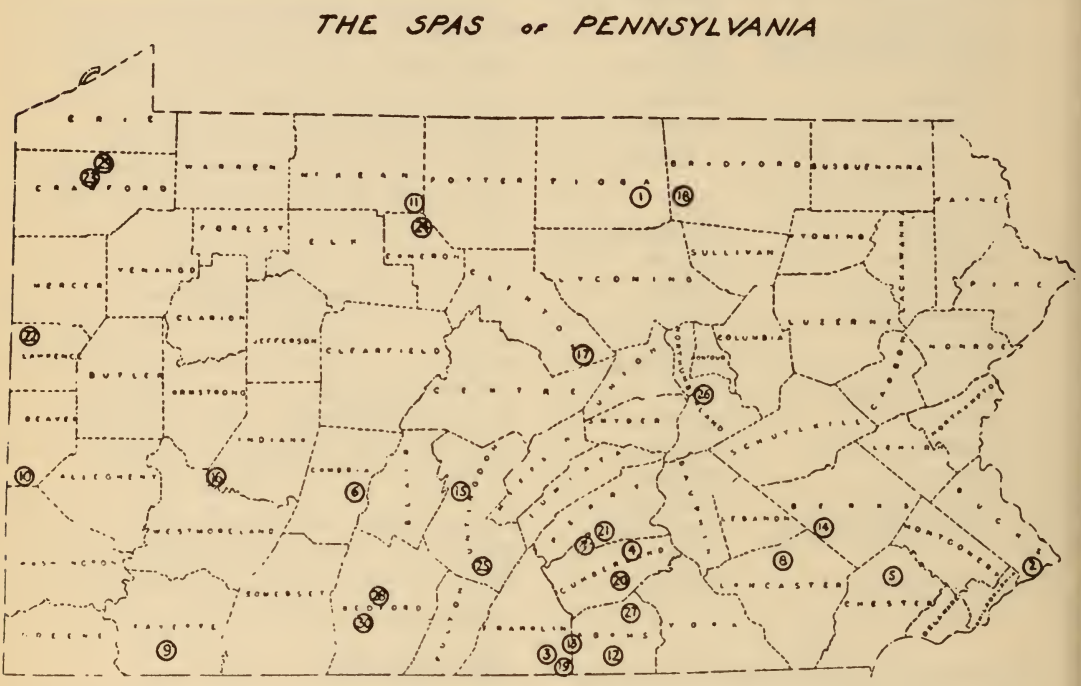

Fig. 1. Map of the Spas of Pennsylvania.
The numbers correspond with those on Table 1.

nearly half a century apart, probably were correct, as wells might have been added to increase the insufficient water supply from the spring. In 1773, versatile and talented Dr. Benjamin Rush praised the virtues of the chalybeate water of Bristol Bath, at that time one of the best known spas on the North American Continent. Rush, along with Drs. William Hewston and Joseph Minnick did much to extend its popularity and reputation. Hewston erected a large bath house in 1807. Shortly thereafter, Minnick built a hotel and race track.

Shelton (12) quoted a passage of a letter from Dr. John A. deNormandie to Dr. Bond of Philadelphia, which stressed the efficiency of the water at Bristol as follows: "It is a cheer of the spirits, a valiant tonic, a powerful alterative, and deobstruent and deserves the ampliest trial from many a distressed, dyspeptic and gloomy son of Spleen. Let, therefore, the votary of midnight excess and the pining invalid repair to Bristol. . . ."

Bristol Bath developed into a gay cosmopolitan resort, attracting many American and foreign personalities of note. Joseph Bonaparte, King of Naples and Spain, an older brother of Napoleon Bonaparte, who, after the fall of the Napoleonic empire, resided across the Delaware River in Bordentown, New Jersey, visited Bristol Bath arriving in a luxurious barge, a gift of his wealthy patron, Stephen Girard. Prince Murat was another visitor of distinction. Saratoga Springs in New York State, by the end of the last century, with its superior natural resources, better facilities for entertainment and hotel accommodations and the allurement of excellent horse racing, finally diverted many guests from Bristol Bath, thereby contributing to its abandonment and final ruin, after a century of successful existence. The old hotel, the bath house, the springs, and wells have long since vanished. Even a commemorative stone marker erected in their place has been removed and lost. On the property of the once famous Bath Springs there now arise, like a phoenix from the ashes of the past, the walls of a modern new hospital soon to be dedicated. The new institution will bear unchanged the motto of its predecessor, "In the service of suffering humanity."

A number of other springs, in and around Philadelphia, came into prominence by the end of the 18th and the beginning of the 19th century (13). Benjamin Rush (14) discovered what was regarded as a mineral well at 6th street near Chesnut Street, on the property of John Lawrence. Fortunately, the well was abandoned before any great damage was done, when it was noticed that the source of its mineral content was sewage contamination.

Dr. James Mease, quoted by Hotchkin (15), knew of two more medicinal springs in 1811; "the Chalybeate water at *Abington*, highly useful for pure debility, jaundice, etc," and another, "a fine spring, impregnated with iron and an adjacent spacious bath house, where you can be well entertained," known as the *Willow Grove Springs*, owned by George Rex. It seems that the proprietor of the Willow Grove Spring occasionally felt the sting of slandering tongues. Shelton (12) quoted an advertisement of July 22, 1811 in which Rex "has the satisfaction to assure the public that the ineffective attempts to injure the reputation of the mineral spring have proved abortive; that it has lately been cleaned and the water analyzed and found to contain aerated vitrolated iron, the presence of which is known by the ochre which it deposits, its taste, the black color which it strikes with astringents and the blue color produced by phlogisticated alkali. . . ." The ultimate fate of both springs is not known with certainty. The authors were unable to find any trace of either spring.

A health resort five miles from the center of Philadelphia at *Harrowgate*, near Frankfort Road achieved considerable popularity thanks to Rush. His directions for "the use of the mineral water and cold bath at Harrowgate near Philadelphia" induced many people to sojourn there. At Harrowgate a swimming pool and a hotel with two showers, both on the estate of George Esterly were supplied with

water containing iron and "hepatic air". Drs. Moyes and Rush recommended this busy spa after a thorough examination of its mineral resources. Prevention of abortion and improvement of conception were credited by Rush to the cold bath of Harrowgate. Literature does not mention if any other methods were used in conjunction with the "hepatic air", for removal of barrenness.

Shelton (12) mentioned *two additional baths:* on a farm belonging to Dr. John Kearsley between Second and Third Streets near St. John Street and the other in Northern Liberties. The latter, owned by John White, provided patrons with hot baths, "tea, coffee, and chocolate with plenty of good cream, etc." It seems that White, assisted by his wife, featured in 1765 a bath house supplied with non-mineralized water. Two hundred years ago, bathing was a formality, not the hurried, casual procedure of today. It required hours, even a full day, plenty of food, music, and a good rest afterwards. A bath was a luxury enjoyed by relatively few adults.

In recent years, within Philadelphia, a number of springs have been found to possess properties heretofore unsuspected. Bohn and Nadig (16) have discovered a number of radioactive springs in Fairmount Park. One spring in Wissahickon, situated only a few miles to the northwest of the center of the city of Philadelphia, contains sufficient amounts of radon to classify it as a strongly radioactive cold spring. The water of the Wissahickon spring contains 240×10^{-10} c/l or 65.93 Mache units of Radon. A partial analysis made by the State Laboratory in 1951–52 revealed an

Alkalinity	26	
pH	6.1	
Hardness	160	
Chloride	49	p/m
Sulphate	94	p/m
Aluminum	0.3	p/m
Calcium	30	p/m
Magnesium	21	p/m
Fluoride	none	
Chromium	none	
Copper	none	
Iron	none	
Manganese	none	
Barium	none	
Total Solids	300	p/m

As far as could be ascertained, no clinical tests have ever been conducted with the water from this Wissahickon spring. The spring is publicly owned, and the water is extensively used by the people of the neighborhood.

Blossburg—Tioga County

Located on a steep hill in back of and above the Blossburg State Hospital, are two springs about 50 feet apart. The upper one, a magnesia spring, was never used therapeutically. The lower one, called Ben-Alan, a very productive spring, carries water of a peculiar acid taste. The entire property is a part of the Gaylord estate. Jacob Jones, grandfather of the present owner (17), acquired the grounds in 1849. The mineral water was used extensively for drinking and sitz baths from 1924 until 1928. The baths were administered in a rather primitive bath house at some distance from the spring. The water was carried and heated on coal stoves. The bottling was continued until 1929. All commercial and therapeutic activities were discontinued after the death of Benjamin F. Jones.

Felix von Oefele, M.D. of New York and Dr. Kjelgaard highly praised Ben-Alan spring. In a lengthy article in the *Blossburg Herald* of June 30, 1927, Dr. von Oefele compared this water with the water of Levico, a noted European spa. Von Oefele warned against the indiscriminate drinking of the Ben-Alan water because of its arsenic contents, which in his opinion could be harmful. The Ben-Alan spring was analyzed by F. A. Genth in the chemical laboratory of the University of Pennsylvania. Concerning his findings, Genth had the following to say: "I have just finished the analysis of the Ben-Alan chalybeate spring and have found it to contain in one gallon of 231 cubic inches, as follows:

Silicii acid	2.15386 grains/G
Sulphuric acid	5.64348 grains/G
Ferrii phosphate	0.32738 grains/G

Ferrii sulphate	31.31905	grains/G
Aluminum sulphate	6.58489	grains/G
Nickel sulphate	0.35819	grains/G
Cobalt sulphate	0.03019	grains/G
Manganese sulphate	1.83367	grains/G
Magnesium sulphate	13.10151	grains/G
Calcium sulphate	23.12789	grains/G
Lithium sulphate	0.11652	grains/G
Sodium sulphate	0.26646	grains/G
Potassium sulphate	0.24442	grains/G
Sodium chloride	0.10128	grains/G
Specific gravity	1.0033	grains/G
Total Solids	85.20879	grains/G

(1.458.78 p/m)

The bath house has been completely destroyed and there is no intention on the part of the owner to attempt any reconstruction.

Caledonia Springs—Or Sweeney's Cold Springs, Adams County

Caledonia Springs or Sweeney's Cold Springs are located south of the Knob in the vicinity of Mt. Alto Sanatorium. A few fragments of the stone foundation of the Caledonia Springs Hotel are discernible between dense woods. The trail to the spring and the site of the former hotel are hardly visible.

The history of the hotel is shrouded in mystery. Neither the year of its origin nor the time of its destruction could be established. According to local information, the hotel burned down long before the beginning of this century. Even the location of the ruins and of the spring is known only to very few. Caledonia Springs Hotel featured some forms of hydrotherapy similar to the procedures used at the Graeffenburg Inn.

The basin of the spring is still relatively well preserved. The tasty, cold, and odorless water does not leave any sediment. No analysis is available.

Carlisle Springs—Cumberland County

The first hotel for the accommodation of summer guests, a two story building, was constructed in 1830 by William Ramsey.

Sulphur springs on Ramsey's property supplied the guests with mineral water. After his death in 1832, David Carnman took over this resort. The fate of this hotel is unknown. It was probably destroyed about 1855 or 56. On June 20, 1857 the Messrs Owen and Chandler opened on the same grounds a new hotel, which was much larger, having three stories with many dormer windows on the fourth floor. Owen and Chandler announced the opening of the new institution as follows:[2] "Carlisle Springs will be opened to visitors on the 20th day of June (1857). This beautiful watering place is situated . . . midst the finest mountain scenery, surrounded by a dry and bracing atmosphere.

"The soil of this region is slate and sandstone and the water, consequently soft. There are several mineral springs impregnated with white sulphur, iron, magnesia, and other minerals; the water of which differs in quality and is superior for drinking and bathing. . . . Carlisle Springs offers many attractions to families and persons desiring a quiet and retired summer retreat, so late as the month of October in an atmosphere particularly salubrious and free of miasma.

"Among the enjoyments at Carlisle Springs are picturesque mountain scenery, fine drives, pleasant walks, and a good table, also a fine band of music, bowling and the customary amusements of watering places . . . Visitors leaving Philadelphia in the morning, will reach Carlisle at 2 o'clock P.M., from thence by hacks, a distance of five miles. . . .

"The fare from Philadelphia to Carlisle is $3.35. . . . Terms—board for first and second week $10.00, board per week by the month, $9.00, board by the day $1.50. Children under 12 years and servants half price."

The second hotel burned down in 1867 and was replaced by a new but smaller unit. All three hotels received guests from 1830 until 1879. The summer guests, sick and well alike, used their available mineral water for drinking and bathing.

The third hotel was acquired in 1880 by Wilson W. Gutshall, who tore it down and erected a farmhouse on this site. It is evident from Bell's statement (18) that Carlisle had

[2] Courtesy Mrs. Annie C. Brindle.

two sulphur springs. It seems that one of the springs ceased to produce, as the descendants of W. W. Gutshall were unable to locate the second spring.

Chester (Yellow) Springs—Chester County

Yellow Springs, today known as Chester Springs, served the Lenni Lenape and Iroquois tribes long before the first white man set foot on the shores of the Delaware. The medicinal properties of the spring became known as early as 1722 (19). The *American Weekly Mercury* of May 31, 1722 brought Yellow Springs to the attention of its readers. Watson's "Annals" (20) mentioned this place as located thirty miles from Philadelphia in Chester Valley. In 1750, at a time when the population of Philadelphia was below the 40,000 mark, Yellow Springs had already many visitors. The owner of a farm in the township of Pikeland, a Robert Pritchard (21), petitioned "The honourable Justices of the Court of Quarter Sessions to be held for the County of Chester ye 28th Augt 1750" for a license "to keep a house of entertainment at Ye Said Place". Pritchard pointed in his petition to the fact that being the owner of "that medicinal water called the Yellow Spring unto which there is Frequently a Great concourse of People on account of Health and also many other Travailing about their Occasions, on a Publik road . . . had already been at a considerable Charge in building and improveing it to Serve the people." This petition must have been granted as in the same year the one story high log building which served as an inn "doubled already as a public house of entertainment to the satisfaction and ease of the neighbours," (13). Some years later Prichard sold the property to John Bailey, a silversmith of Philadelphia. Bailey constructed a new, larger, and more comfortable inn. The consumption of mineral water and other more intoxicating liquids must have been a part of the general entertainment enjoyed by the thirsty guests but not by the annoyed neighbors. In 1765, the alarmed Friends of Lionville protested in a public meeting for the sake of their own children against the kind of diversion offered in this promiscuous resort. This complaint did not harm the business at the spring. On the contrary, it attracted even more visitors from near and far.

A letter of Hannah S. Skelton to Dr. John Morgan on August 32nd (sic!) 1767 contains valuable information on the hydrotherapeutic routine at Yellow Springs (22). Female inconsistency is shown in two sentences, one at the beginning and the other at the end of her letter. "I have not as yet received any benefit as I can percive . . . but have done very well since." Miss Skelton mentioned three important facts: (1) the unpleasant taste of the water: "It was disagreeable at first, but is very pallittable now"; (2) baths were taken in cold water, which precipitated even an accident on its first use: "I have been in the springs several times and feel very comfortably after I come out. It made me very sick the first morning I went in" . . . "and the water being so cold it proved too strong for me and I sunk down to the bottom and the first I felt was my head against the gravel . . ."; (3) bathing was done in a natural or excavated deep reservoir or creek with gravel on the bottom, accessible by the way of stairs . . . "Had it not been", writes Miss Skelton, "for a resolute young woman bin with me, I believe I should without doubt drowned, but she had the presance of mind and rand down the steps and pulled me out . . .".

On the premises of Yellow Springs, three springs are well preserved. None has a natural reservoir; all are nearly level with the surrounding ground and no stairs are needed to reach them.

In 1774 the name of Dr. Samuel Kennedy appears in connection with Yellow Springs. Kennedy was born at sea in 1730 to David and Margaret Kennedy, emigrants from Downpatrick in Ireland. In 1777, the Continental Congress accepted Dr. Kennedy's offer and authorized the erection of an Army Hospital at Yellow Springs. Kennedy became its first Director and Senior Surgeon. The hospital accommodated not only wounded but also

men suffering from typhoid fever, typhus, and smallpox. On September 17, 1777 General George Washington made his temporary headquarters there. Dr. Kennedy contracted an infection and died on June 17, 1778, at the age of 48. The Hospital burned down on May 19, 1902.

With the return of normal conditions, after the Revolutionary War, Yellow Springs resumed its role as a fashionable spa. Financial difficulties forced frequent changes of ownership. Under all its successive proprietors, the initial project to erect a small town around the hotel with the designated name "Bath" never materialized.

Direct coaches from Philadelphia, running regularly three times a week, brought this celebrated watering place within the reach of a large segment of the population. Boats on the Schuylkill River provided another means of transportation. Many celebrities stopped there to enjoy this "fine scenery", the famous mineral waters, and the joyous entertainment. It is presumed that the beautiful Swedish soprano, Jenny Lind, was once a guest at this spa. In her honor, one of the springs was christened Jenny Lind Spring.

In 1845, Dr. George Lingen acquired Yellow Springs from a Mrs. Margaret Holman. Mrs. Lingen is credited with the discovery of a new spring—the Diamond Spring, while her husband added a new bath house for ladies. Under his management, the female guests were advised to wear for bathing the following costume: "A large morning gown of a cashmere shawl pattern, lined with crimson, a Greek cape, Turkish slippers and a pair of pantaloons". History does not record how much of this elaborate costume was retained in the bath.

A description of Yellow Springs or a hidden advertisement (23) in the *Philadelphia Argus* of July 6, 1855, reprinted in the *American Republican* of July 10 of the same year, corroborates the earlier statements of Miss Skelton, as the writer of this description also mentions, "the bath . . . of coldest water". The contents of this nearly a century old contribution might have been written only yesterday. "At Phoenixville, we left the railroad and mounted a stagecoach for a seven mile ride over one of the hilliest and dustiest roads that we ever recollect to have met with. The driver was courteous and treated us to numerous bits of local history and biographical sketches of the people through whose domain we were passing. Before eleven o'clock we dashed recklessly up to the piazza and were warmly welcomed by Mrs. Neef, the estimable hostess of the Yellow Springs Hotel. It may astonish some who believe in the absolute perfection of the Saratoga and Newport, but we think it is a remark that experience will prove to be true, viz: that there is not on the American Continent a watering place where pleasure is so closely connected with the health-giving applications and where the visitor can more truly enjoy himself than at the Yellow Springs. The coldest conceivable water bubbles up and trickles away, leaving a saffron tint upon the rocks. Copious draughts of this delightful liquid will bring the blush of health to the cheeks of pallid beauty and make the muscle fibre tingle with renewed strength. After a plunge in the bath, a mild exercise in the ten pin alley and a climb to the summit of the hill that rises almost perpendicularly behind the hotel, one is prepared to make a savage onslought upon the good things with which Mrs. Neef's table groans."

Once more, during the Civil War, Yellow Springs came to prominence as a hospital for wounded soldiers. After 120 years, it ceased to play its sometimes stormy part as a spa or hospital. Playground of three generations of prominent Americans and famous for the many historical events which took place within its walls and in close vicinity, Yellow Springs changed after the Civil War to a more quiet and peaceful place, later serving as an Orphan's School, subsequently as the summer school of the Pennsylvania Academy of Fine Arts. Only the well-preserved buildings and the three still producing springs bear witness to its great and enchanting past.

Indifferent to sentiment and not satisfied

with the mere statement of great therapeutic results, modern scientific methods have been employed to evaluate these mineral springs, by the chemical analysis of their water. The following chemical analyses fail to explain the clinical success obtained with these once celebrated waters.

Analysis of the springs at Yellow Springs, Commonwealth of Pennsylvania, Department of Health, Bureau of Sanitary Engineering, Chemical Laboratory, Harrisburg, Pennsylvania, number 33355, January 1952:

Spring "A" Iron Spring

pH	6.7	
Alkalinity	34	
Hardness	64	
Chloride	2.0	p/m
Fluoride	.3	p/m
Sulphate	54.0	p/m
Aluminum	5.5	p/m
Calcium	15	p/m
Chromium	0.0	p/m
Copper	0.03	p/m
Iron Total	4.0	p/m
Magnesium	6.5	p/m
Manganese	0.4	p/m
Barium	0	p/m
Total Solids	145	p/m

Spring "B" Sulphur Spring, same laboratory #33356, January 1952

pH	7.1	
Alkalinity	48	
Hardness	110	
Chloride	2.0	p/m
Fluoride	0.1	p/m
Aluminum	4	p/m
Calcium	26	p/m
Chromium	0	p/m
Copper	0.03	p/m
Iron Total	3.0	p/m
Magnesium	12.0	p/m
Manganese	0.3	p/m
Barium	0	p/m
Total Solids	180	p/m

Spring "C" Diamond Spring, same laboratory, #33357, January 1952

pH	6.9	
Alkalinity	50	
Hardness	62	
Chloride	4.0	p/m
Fluoride	0	p/m
Sulphate	3.0	p/m
Aluminum	0.3	p/m
Calcium	19.0	p/m
Chromium	0	p/m
Copper	0	p/m
Iron Total	0	p/m
Magnesium	3.5	p/m
Manganese	0	p/m
Barium	0	p/m
Total Solids	110	

Cresson Springs—Cambria County

Cresson was settled in 1788 or 1789. The transition to a resort occurred as early as 1818, with the opening of the first Inn and Tavern by Jacob Troxel, for the changing of horses and the accommodation of guests and travelers. In 1835, Dr. Jackson, a physician from Philadelphia, acquired this tavern. His friend and frequent visitor, a Mr. Cresson, gave the name to the settlement. Cresson, the birthplace of Admiral R. E. Peary, the discoverer of the North Pole, was immortalized by Charles Dickens, who vacationed here while visiting America. Here he wrote of his trip on the "Old Portage" railroad from Holidaysburg to Conemaugh. The original Portage Railroad was put in operation in 1833. It was replaced by the Pennsylvania Railroad, which reached Cresson in 1854 after mastering considerable difficulties which led to the construction of the famous Horse-Shoe Curve.

Two of the old hotels, the Stone House and the Linton Hotel are still in existence, but the Dividing Ridge, a hotel of 80 rooms, was lost by fire in 1889.

The Allegheny Mountain Health Institute[3] was incorporated 100 years ago on the 29th of April, 1853. In the early 50's of the last century, the Pennsylvania Railroad erected a wooden hotel building at Duncanville, which prospered for three years. It was then taken apart and moved to the grounds of the Health Institute, forming the nucleus of the later well-known "Mountain House". In 1861 the name of the company was changed to "Cresson Springs Company." This company was in-

[3] We are indebted for this information to Ralph C. Champlin, Vice-President of the Pennsylvania Railroad Company.

corporated for the purpose of constructing and operating a place for recreation, convalescence, a museum, library, observatory, and other facilities for the promotion of natural sciences. In 1880 the Cresson Springs Company owned approximately 200 acres on the summit of Allegheny Mountain at Cresson. Many additions were made to the original Mountain House and other supplementary buildings were constructed from time to time. A ballroom, bar, ice cream salon, and removal of the "old water closet" were planned already in 1859. At about 1880, the Mountain House had 89 rooms, accommodating 100 to 125 people, besides many cottages on the land belonging to the company. The hotel operated at a profit until 1885, but thereafter continued at a deficit. In the early 80's, an entirely new and modern resort hotel was constructed at a total cost of a quarter of a million dollars. This new hotel could accommodate 600 persons. At this time, the Pennsylvania Railroad owned nearly the entire stock of the Cresson Springs Company.

The year 1898 was a critical one in the history of the Company. Financial failure and sale of the property sealed the doom of the famous spa. The hotel was permanently closed; the Cresson Springs Company was dissolved in April, 1911 and the building torn down and dismantled in 1917 by Peter Cassidy.

Of the palatial hotel and its bath house, only a few foundation stones are still visible. The mineral springs are grossly neglected and probably contaminated.

It seems that the Pennsylvania Railroad selected the site for a resort hotel at Cresson only after abandoning an original project to acquire the Warm Springs of Huntingdon. The intentions of a Mr. Wilson of Huntingdon, the owner of this old and renowned spa, to capitalize on the plans of the railroad, may well have been responsible for the railroad's final choice of Cresson.

The mining activities of this region and the heavy smoke of the railroad yards at Cresson interfered seriously with the comfort of the guests and were in large measure responsible for the final failure of this hotel.

In the vicinity of Cresson, less than a mile away, are two other mineral springs supposedly of some medical significance. A third one, the Prince Gallitzin Spring, is still productive and well preserved. This historically important spring was never used therapeutically. Identification of the several springs said to contain "pure iron, alumina, and magnesia" is impossible at present without a new analysis of these waters.

Doubling Gap—Cumberland County

The history of Doubling Gap goes back to 1791, when it was known as McFarland's Gap. Despite the sparse population McFarland's Gap had already in 1800 summer guests at the "Fruit Farm". The following years brought a great influx of vacationists and patients to this place. In 1846 the Fruit Farm was enlarged and ten years later completely rebuilt and a new stone building added.

Doubling Gap Hotel, a large building, was modernized at different times. The central part is the original stone house erected by Scott Coyle around 1856. It has over 100 rooms and other accommodations. The hotel serves now as a retreat for the members of the Church of God.

A few hundred feet below the hotel there are a number of well preserved mineral springs. The first three were used extensively in the past for medicinal purposes, and even today these waters are in demand and are recommended by some older practitioners in this region. The first spring, at the foot of a steep path from the hotel, is the sulphur spring; a few hundred feet farther are the iron and magnesia springs. Two springs are well protected by wooden spring houses.

According to Rischel (24) the water of two springs was analyzed by Professor James C. Booth, Chemist of the United States Mint in Philadelphia. The analyses of the springs show that:

Spring Number 1, known as Sulphur Spring contains:
Sulphurated (sulphuretted) hydrogen
Carbonate of soda and magnesia
Glauber salt
Epsom salt
Common salt
Carbonic acid
Alkaline reaction

Spring Number 2, so-called Chalybeate Spring contains:
Bicarbonate of iron (as chief characteristic)
Epsom salt
Common salt
Carbonate of magnesia

The seclusion and peace of this idyllic spot was frequently and vehemently interrupted by the "Robin Hood of Pennsylvania", the colorful David Lewis. He is referred to by D. D. Rischel (24) as a "robber and counterfeiter, the terror of the Cumberland Valley". His deeds are still more vivid in the memory of the local inhabitants than the therapeutic achievements of Doubling Gap. Lewis, who called himself an "equalizer", practiced a form of communism. He invariably centered his criminal attention on the well-to-do and apparently shared a part of his loot with the less fortunate settlers. The radius of his activities included nearly all of central Pennsylvania. Well known is his holdup of a post coach near Cresson Springs. It seems that he enjoyed the support of many sympathizers who supplied him with food and information when Lewis, hard pressed by the authorities, retired to the wooded hills. Peace returned to Doubling Gap when justice finally caught up with him.

Ephrata—Lancaster County

Ephrata, once a widely known resort, still boasts of a well preserved hotel, The Mountain Spring House. Formerly this was a "popular and fashionable resort" . . . "patronized by many prominent people" (25).

The large building was erected in 1848 by Joseph Konigmacher and enlarged substantially about two years later (26).

"Previous to this, the place had been occupied as a water-cure or hygienic home for invalids." The partly modified buildings occupy more than a city block but have been closed for many years.

Fayette Springs—Fayette County[4]

Deep in the woods at the foot of the west slope of Chestnut Ridge in the Laurel Mountains, at a distance of about three quarters of a mile from U. S. route 40, is a small spring, the sole remnant of a once well known watering place. An antique canopy supported by a small back wall and in front by two old columns covers the main spring. A second outlet of the same spring emerges only a few feet away. The Fayette Springs are seriously neglected. The lack of drainage has converted the surrounding grounds into a veritable swamp, covered by high grass and dense underbrush. Located on the east side of the dirt road from Chalk Hill, close to a creek, this marsh is the gathering place of an assortment of small animals and insects which enjoy here protection in undisturbed peace. The brackish water has a slightly alkaline aftertaste.

Fayette Springs was known to Indian Tribes, who respected its powers by abstaining from war in its vicinity. It was the white man who brought devastation and suffering to this area. British troops under General Edward Braddock operated in this region in June, 1775 in their campaign against Fort Duquesne held by the French and their Indian allies. A trail, afterwards known as Braddock's Road, is preserved here. Tom Fawcett, the man who allegedly shot and killed General Braddock after his historic retreat from Fort Duquesne, owned a tavern only a few miles away from here. General Braddock is buried about one mile from this spring. On July 14, 1775 the last rites were read at his grave by his aide-de-camp and subaltern officer, Lt. Col. George Washington, who covered the British retreat with his detachment of Volunteer Virginia riflemen.

[4] The authors are grateful to S. A. Baltz, M.D., Chief Health Officer of Fayette County, Mr. Wortley of the Uniontown Water Company, Miss Markle, Mr. J. T. Ruby, all of Uniontown and Dr. Sherry of Hopewood for their help and friendly cooperation in obtaining the data on Fayette Springs.

According to Ellis (27), a Dr. Daniel Merchant of Uniontown analyzed Fayette Springs in 1814 and reported it "as valuable". Ellis, who knew about therapeutic springs in this part of the country, stated: "Mineral springs of reported curative properties exist in several places—a large sulphur spring at Baumgartner's near Gibbon Glade, Chalybeate Springs at William Smith's on the turnpike, a very strong sulphur spring near Farmington and the celebrated Fayette Spring near Chalk Hill on the National Road . . .". The author mentioned that the Fayette Spring was a "strong sulphur spring". There is reason to believe that a log cabin or inn preceded the hotel built in 1822. In 1860, there was a substantial hotel with a post office. Two to three hundred summer guests visited the hotel annually. Fayette Springs Hotel was a large two story stone house intended as a summer resort and not for year round use. It was built by the contractor Charles McKinney, under the direction of the Honorable Andrew Stewart. The date of the destruction of the hotel is not known exactly. It seems that the hotel burned down at about 1880. A number of the remaining stones from the old hotel building adorn Mr. Ruby's summer home and its walks.

The country around Chalk Hill has many springs, once essential sources of water, along the highly traveled old National Road. Washington Spring at some distance and Monroe Spring on the side of the road are perhaps the best known. Important events which led to the birth of the United States are closely associated with the history of two spas in Pennsylvania, Yellow Springs in Chester County and Fayette Springs on Chalk Hill.

Frankfort Springs—Hookstown, Beaver County

Named for a suburb of Philadelphia, Frankfort Springs is about 26 miles northwest of Pittsburgh. The hotel erected about 1870 used mineral water for therapeutic purposes. The hostelry had 38 rooms, 1 cottage with 8 rooms, a ballroom, and facilities for bowling. In the late 1870's a second Hotel, Hotel Vanice, was erected at the southern entrance of Frankfort. Mineral water was hauled into the hotel from the springs. The substantial brick building is now used as a family dwelling and known by the name of Pain Knoll Lodge. The springs are located in the Racoon State Forest about 1000 feet from the main road, accessible over a dirt road and a steep narrow path. Both springs are at the entrance to a rocky cave. No analyses are available, but according to the statement of an octogenarian residing in Frankfort Springs, Mr. Harry Stevens, the mineral waters contain magnesia and are laxative. Frankfort Mineral Springs Hotel was destroyed by fire about 17 years ago and not even traces of the foundations could be found at its former site.

Gardeau, Parker Mineral Springs—P. O. Keating Summit, McKean County

Gardeau had only a short period of prominence as a spa. Naturally endowed with mineral water of unusual qualities and pleasant surroundings, it attracted a Mr. Parker, an enterprising Canadian, who settled here. Under his direction, a hotel sanitarium, and a wooden bath house in back of the hotel were constructed in 1890. The mineral water was bottled and shipped as far as Europe. According to Mrs. Kathryn L. Witmer, one of the oldest inhabitants of Gardeau, Parker, a devoted subject of His Majesty, sent a number of bottles of this water to the British King. The hotel and sanitarium consisted of a large brick building of three stories, with a porch and balcony across the front and a solarium on the roof. The hotel was destroyed by fire in 1894 and never replaced. Three trees planted by Parker in front of the building grew to stately proportions and are today the sole remnants of the Mineral Springs Hotel. Only a few stones and some of the foundation are left. The spring is quite neglected and hidden by tall weeds and heavy underbrush.

The following analysis was quoted by Fitch (28). Analyzed by Henry Trimble, it shows the following hypothetic combinations:

Potassium chloride	Trace
Sodium chloride	4,831.60 p/m
Magnesium chloride	1,878.26 p/m

Calcium chloride	3,794.83 p/m
Calcium bicarbonate	331.03 p/m
Silica	22.74 p/m
Total solids	10,858.46 p/m

Gettysburg Katalysine Spring[5]*—Adams County*

Little known before 1863, Gettysburg Katalysine Spring achieved fame during the Civil War. An historical event of the Civil War led to its popularization.

A unit of the Confederate Army had its camping grounds near the Spring in June or July 1863. As a result of the summer heat, the soldiers drank freely of the water from the cold, sparklingly clear spring. There promptly followed a disabling outbreak of profuse diarrhea. Unacquainted as they were with the effect of laxative mineral waters, the soldiers blamed the Yankees for this intestinal disorder. Their field surgeons assumed that the unfriendly, infuriated population had poisoned the spring. Because of this occurrence the waters of the katalysine spring gained a fame which lead after the Civil War to the erection of a large hotel with a high cupola overlooking the battlefield of Gettysburg. This hotel was situated about 500 yards southwest of the spring known previously under the name of Gettysburg Spring. The hotel had accommodations for about 300 guests. The mineral water was used initially for bathing and drinking. Under the management of its first director, a physician, the institution was apparently very successful. A horse drawn trolley operated from the center of Gettysburg to the spring hotel.

The therapeutic use of the katalysine spring was abandoned after a decade, but its bottled water was sold for a number of years. In the years following its construction the hotel changed hands many times. The Spring Hotel, after it ceased to be used as a spa, became mainly a summer resort until 1900, when it was permanently closed. After the First World War, the abandoned hotel was completely destroyed by fire.

The spring, now situated on the grounds of the Gettysburg Country Club, on the edge of the golf course, was used until 1950. Dissatisfied with the insufficient quantities of water available for showers and baths, the management of the club enclosed the spring and thus abandoned one of Pennsylvania's more effective mineral sources.

In 1876, in his inaugural speech, as President of the Adams County Medical Society, O'Neal compared the water of the Katalysine Spring and its therapeutic indications with the famous springs in Carlsbad, in what was then known as Austria, Kissingen in Germany, and Vichy in France. O'Neal (29) deplored the fact that his confreres never attempted to learn anything about the use of mineral waters for the benefit of their patients. According to O'Neal, Katalysine Spring contained lithia, bicarbonate of soda, bicarbonate of potassium, magnesia, bicarbonate of lime, etc., traces of chloride, phosphate, iron, and silica were present. From his speech it is evident that the Gettysburg Katalysine and Lithia Spring are identical.

Many years later the value of hydriatic procedures was emphasized by Coulter (30) in the following sentence, "The history of the use of water as a remedy serves to direct attention to an attitude of the medical profession which still persists. A simple agent, such as water, which is cheap and easily available, is often neglected for a complicated system of therapy which is not so effective."

Graeffenburg Inn, Caledonia, P. O. Fayetteville —Franklin County

Graeffenburg Inn, a connecting link between Adams and Franklin Counties, is situated on the main road, 14 miles west of Gettysburg. In 1800, a simple log building housed here a tavern shrewdly built by an Alexander Caldwell across the boundary line dividing Adams and Franklin Counties. It became a center of humming activity, being a preferred stop for tired and thirsty travelers. For many years,

[5] We are indebted for the information concerning Gettysburg to Dr. Henry Stewart of Gettysburg, a graduate of the University of Pennsylvania of 1892.

this tavern with its movable bar was a thorn in the side of the everwatchful tax conscious authorities, whose revenuers tried in vain to collect the levy on whiskey. General Early, moving towards Gettysburg in 1863, destroyed the tavern and the vitally important iron furnaces at Caledonia. The inn was rebuilt by Edward McPherson. The name of Graeffenburg was selected by McPherson in honor of a small town in Silesia, a province of the then Austrio-Hungarian Empire. In the original Graeffenburg, there was a famous institution of hydrotherapy, founded by Priessnitz. The new inn followed the procedures of the celebrated Priessnitz, which were carried out in a special bath house.

It is certain that some types of water treatment were cultivated at Graeffenburg long before the erection of this hotel. An advertisement in the Gettysburg Compiler of May 8, 1848 invited the public to take a water "cure" in the newly completed building. The proprietor, David Goodyear, also announced the impending opening of a two story "Mansion House" of 40 by 90 feet for the accommodation of visitors. In the same advertisement the public was warned against the danger of indiscriminate bathing without the advice and direction of an expert. Nine years later this Inn had a total of 19 rooms; a post office was established there in October, 1849. The present Graeffenburg Inn is a product of the 1920's and as such is not concerned with hydrotherapy.

Grand View Sanatorium, Pavillon Spring, Wernersville, Berks County

Pavillon Spring (28) in Berks County is located on the premises of the former Grand View Sanatorium owned by Reuben D. Wenrich, M.D. and later by his two sons, Drs. Geo. A. and John Adam Wenrich. This sanatorium is located on a slope of the south mountains slightly over two miles south of Wernersville, and about eleven miles west of Reading, at an elevation of 900 feet above sea level. On clear days, the fertile Lebanon Valley, the City of Reading, the Blue Mountains, etc., are clearly visible. Grand View had an excellent water supply, a large reservoir, and a nonsectarian church. Established in 1847, this elaborate medical institution was developed and enlarged many years later by Dr. R. D. Wenrich, an untiring physician and administrator. Grand View offered not only splendid vistas, but also modern comfort. Medical treatments there featured elaborate physical and hydrotherapy, which included nauheim, steam, and sulphur baths, and therapeutic exercises. Pavillon Spring supplied water of low mineralization, which was in great demand by the majority of patients. According to Dr. Wenrich, cool beer was preferred by some of the guests. The following analysis was supplied by John Adam Wenrich, M.D.:

Sulphate of potassium	3.00 p/m
Sulphate of soda	0.30 p/m
Chloride of soda	1.10 p/m
Carbonate of soda	5.60 p/m
Carbonate of lime	4.00 p/m
Carbonate of magnesia	2.1 p/m
Alumina and oxide of iron	Trace
Silica	16.2 p/m
Organic and volatile matter	1.7 p/m
Total solids by evaporation	34.00 p/m

This elaborate medical installation was sold a few years ago and is being converted into apartment houses.

(The concluding installment of this paper will appear in a subsequent issue.)

Memoir of Alexander Randall (1883-1951)*

By CHARLES A. W. UHLE

OUR late distinguished and beloved member of the College of Physicians, Dr. Alexander Randall, passed away quietly at his home in Chestnut Hill, Philadelphia, on November 18, 1951. Stricken by a vascular accident in the prime of his life and at a time when he had reached the enviable goal of greatness in his chosen field, he accepted the last years of his life with courage and dignity.

Dr. Randall was born in Annapolis, Maryland on April 18, 1883. He spent his boyhood and received his early education in that area graduating from St. John's College Preparatory School in 1897 and from St. John's College, Annapolis in 1902 with a Bachelor of Arts degree in Latin. He was the youngest member of his class.

Having been reared along the shores of Maryland it was quite natural that he should become imbued with a love for the sea at an early age. Ships and sails were his avocational delight throughout his life. At the age of twenty he joined the Bahama Expedition and for three summer months cruised and explored under the auspices of the Maryland Geographic Society. In later decades he was to skipper his own boat, cruising with his family along the New England seacoast during his summer vacations. Shortly before his death, I visited Dr. Randall and found him perusing the earliest "Proceedings of the Corinthian Yacht Club" of which club he was an enthusiastic member. He often took the helm in many of its regattas and races.

Dr. Randall's medical career began with his graduation from Johns Hopkins Medical School in 1907. He was next to the youngest member of his class. Shortly after graduation he was also granted a degree of Master of Arts by St. John's College. By timely coincidence and fortuitous family combination his father, John W. Randall, also was granted a Master of Arts degree on the same day and by the same college. These were no idle days for the recent graduate who had received his indoctrination in the Halls where Osler, Welch, Halstead and Kelly taught. Dr. Hugh Hampton Young, who was younger than the immortal four and associated with them at Hopkins in their pioneering work, also left an imprint upon the impressionable young surgeon.

Dr. Randall next ventured beyond the Mason-Dixon line to assume his duties as resident at the German Hospital (now Lankenau) in Philadelphia. Here his surgical appetite was further stimulated by Dr. John B. Deaver who was at the height of his dynamic career and who had a penchant for genito-urinary surgery, as it was called in that era. It is of historical medical interest and a tribute to Dr. Deaver that four of Dr. Randall's contemporaries at the old German Hospital, Dr. Wilbur Haines, Dr. Leon Herman, Dr. William H. Mackinney and Dr. Alexander A. Uhle should also elect Urology as their chosen field and should all practice in the city of Philadelphia.

Following his residency, Dr. Randall journeyed back to Baltimore to become Hugh Young's private office assistant, and subsequently, on December 1, 1910 to enter Johns Hopkins Hospital as assistant resident surgeon in charge of Urology. He was the first resident to get full recognition of such duties and he served in this capacity for two years. In Baltimore lies the corner-stone for the modern edifice of Urology, the foundations of which were laid, at the turn of the century, by Hugh Young. Dr. Randall was one of his earliest disciples and was included among the twenty-nine residents to whom Dr. Young paid tribute in his book "Practice of Urology" for their achievements and their distinguished urologic teaching positions in medical schools the length and breadth of the United States.

* Read before the College of Physicians of Philadelphia, 1 April 1953. Prepared and published at the request of the Council of the College.

Dr. Randall retraced his steps to Philadelphia to start practice in January, 1912. He limited his clinical work entirely to Urology and stimulated his investigative spirit by accepting an appointment as Assistant Pathologist to the Children's Hospital for a period of three years. During his thirty years of active practice he served at one time or another on the staffs of the Abington Memorial Hospital, Bryn Mawr Hospital, Chestnut Hill Hospital, Germantown Hospital, Graduate Hospital, Hospital of the University of Pennsylvania and Mt. Sinai Hospital. This is an imposing list of distinguished institutions which would have exhausted a man of lesser stature and endurance. In addition to his clinical work, Dr. Randall was always projecting his thoughts to the solution of problems in the investigative field of Urology. His two great monumental contributions for which he will long be remembered relate to the etiology of renal calculus formation and the pathologic obstructions of the prostate. His one published book, "Surgical Pathology of Prostatic Obstructions", is a masterpiece. Published in 1931 it is still sought by students and all urologic bibliophiles. Its contents today are still as fresh and basic as when first written a little less than twenty-five years ago. He contributed numerous articles to the urologic literature and travelled extensively in this country as guest lecturer and speaker.

In 1912 Dr. Randall was appointed Assistant Instructor of Surgery in the Medical School of the University of Pennsylvania and served continuously, until his retirement in 1944, on the staff of the University except for one year during World War I. In the spring of 1918 he sailed for France with the University of Pennsylvania Hospital unit. During the course of his duties abroad, Hugh Young, consultant to the American Expeditionary Force, heard of Dr. Randall's presence so that it was not long before he was transferred to the 35th Division as consultant, and in turn transferred to the Third Army. Following cessation of hostilities, he served several months with the Army of Occupation in Luxembourg.

In 1929 Dr. Randall was promoted to the Professorship of Urology in the Medical School of the University of Pennsylvania. For fifteen years he influenced and taught countless numbers of young men. His lectures were among the most popular at the University. He could count on a full complement of students at every lecture, even from 11:00 a.m. to 12:00 noon on a Saturday morning prior to a football game. His rhetorical ability, powers of expression and full resonant voice produced a fine orator and delighted his audience.

In 1935 Dr. Randall was certified to Founder Membership in the American Board of Urology. His affiliate memberships in medical and lay organizations are too numerous to recount. His election as President of the American Urological Association in 1931, President of the American Association of Genito-Urinary Surgeons in 1937 and as Fellow of the American Surgical Society and the American College of Surgeons were fitting tributes to his leadership and ability, his friendly disposition and affable personality.

No man's biography is complete until the personal side of his family life is told. The basic strength of America lies in the integrity of the family unit. There could never have been a more staunch supporter of this fundamental axiom than Dr. Randall. In 1915 he married Miss Edith T. Kneedler of Chestnut Hill, Philadelphia. To them three children were born, Alexander, Peter and Virginia. Dr. Randall lived to see his two sons become physicians and his daughter a nurse. This gentle, well-bred man of Annapolis was steeped in family tradition, and happily lived long enough to become a grandfather.

In recent years we have heard the phrase used with political connotations that "old soldiers never die." That same spirit applies to sailors as well. Alexander Randall was a seafaring man carrying with him all the traditions of the respected Captain—character, leadership, keen intellect, a searching eye for scientific truths lying beyond the horizon, devotion to the duties of his profession, and loyalty to his family, friends and colleagues.

Transactions of the Sections

SECTION ON GENERAL MEDICINE

26 January 1953

Nickel Poisoning with Particular Respect to Nickel Carbonyl. F. William Sunderman, M.D., and J. F. Kincaid*, PH.D. (Discusser: F. Curtis Dohan, M.D.) (*Abstract 1, below*)

Diffuse Collagen Disease Complicating Malignancy. John Lansbury, M.D. (Discusser: Karl E. Paschkis, M.D.) (*Abstract 2, below*)

The Clinical Value of Tests for Ketonemia in the Diagnosis of and Treatment for Diabetic Coma. Garfield G. Duncan, M.D., and Kenneth R. Knox*, M.D. (Discusser: Joseph T. Beardwood, jr, M.D.) (*Abstract 3, below*)

A New Classification for Coronary Disease Based on Necropsy Study of 250 Patients: Its Relevance to Electrocardiographic and Clinical Diagnosis. John J. Saÿen, M.D., Warner F. Sheldon* M.D., and Charles C. Wolferth, M.D. (Discusser: Joseph B. VanderVeer, M.D.)

23 February 1953

The Incidence of Endocrine Dysfunction following Postpartum Hemorrhage and/or Shock. Norman G. Schneeberg*, M.D., William H. Perloff, M.D., and S. Leon Israel, M.D. (Discusser: J. Robert Willson, M.D.) (*Abstract 4, below*)

Gastrointestinal Pressure Recordings in Man—Preliminary Report on Physiological and Pharmacological Aspects. Stanley H. Lorber, M.D., and Harry Shay, M.D. (Discusser: Thomas E. Machella, M.D.) (*Abstract 5, below*)

The Detection of Pre-clinical Carcinoma of the Lung on Routine Chest X-ray. Katharine R. Boucot, M.D., and Martin J. Sokoloff, M.D. (Discusser: David A. Cooper, M.D.) (*Abstract 6, below*)

Diffuse Interstitial Fibrosing Pneumonitis. J. J. Kirshner, M.D. (Discusser: Robert L. Breckenridge, M.D.) (*Abstract 7, below*)

23 March 1953

Coincident Hypertension and Addison's Disease. Alexander Margolies, M.D., Henry M. Wise*, M.D., and William A. Jeffers, M.D. (Discusser: Garfield G. Duncan, M.D.) (*Abstract 8, below*)

The Problem of Gross Gastrointestinal Bleeding. Paul Cimoch*, M.D., Herbert A. Yantes*, M.D., and C. Wilmer Wirts, M.D. (Discusser: Thomas E. Machella, M.D.) (*Abstract 9, below*)

Thyroid Function as Revealed by New Radioactive Iodine Technics. Robert Robbins, M.D. (Discusser: Foster Murphy*, M.D.) (*Abstract 10, below*)

Mitral Commissurotomy in the Older Aged Patient. O. Henry Janton, M.D., Robert P. Glover*, M.D., and Thomas J. E. O'Neill*, M.D. (Discusser: Louis A. Soloff, M.D.) (*Abstract 11, below*)

27 April 1953

The Use of Sodium Dehydrocholate in the Diagnosis of Biliary Tract Disease. Joseph M. Gambescia*, M.D., Charles M. Thompson, M.D., Alex Ulin*, M.D., and William Shoemaker*, M.D. (Discusser: Frank Brooks*, M.D.) (*Abstract 12, below*)

Serum Electrolytes in Uremia. F. William Sunderman, M.D. (Discusser: John Eiman, M.D.) (*Abstract 13, below*)

Total Thyroid Gland Transplant Using Vascular Anastomoses in Treatment of Chronic Tetany. Julian A. Sterling, M.D., and Ralph Goldsmith, M.D. (Discusser: Edward Rose, M.D.) (*Abstract 14, below*)

The Effect of Ganglion Blocking Agents in Congestive Heart Failure. Charles R. Shuman, M.D., Norman Learner, M.D.,

* *By invitation.*

and John N. Doane, jr*, M.D. (Discusser: Louis A. Soloff, M.D. (*Abstract 15, below*)

SECTION ON MEDICAL HISTORY

29 January 1953

THE VANISHING SPRINGS AND HEALTH RESORTS OF PENNSYLVANIA[1]. George M. Piersol, M.D., and Igho H. Kornblueh, M.D.

MEDICAL STUDENTS AND THEIR EXAMINERS IN 18TH CENTURY AMERICA[2]. Whitfield J. Bell, jr*, PH.D.

26 February 1953

A VIEW OF WHAT PRIMITIVE MAN THOUGHT OF DISEASE. Anderson Nettleship*, M.D. (*The Kate Hurd Mead Class of 1888 Fund of the Woman's Medical College of Pennsylvania Lecture in Medical History*)

26 March 1953

THE EXODUS OF THE SOUTHERN MEDICAL STUDENTS FROM PHILADELPHIA IN 1859. Thomas W. Murrell*, M.D.

DR. CRAVEN AND THE SHACKLING OF JEFFERSON DAVIS. Chester D. Bradley*, M.D.

SECTION ON OPHTHALMOLOGY[3]

15 January 1953

OPEN ANGLE GLAUCOMA. W. Morton Grant*, M.D.

19 February 1953

GALACTOSE CATARACTS. Edward Cannon, M.D., and Joseph Ritter*, M.D.

THE SIMULATED PROGRESSION OF VISUAL FIELD DEFECTS OF GLAUCOMA. Robert L. Day*, M.D. (Discusser: Harold G. Scheie, M.D.)

CATARACT IN ALLOXAN DIABETIC RABBITS. David Naidoff, M.D., Arno E. Town, M.D., I. J. Pincus*, M.D., and M. E. Scott*, B.S. (Discusser: I. H. Leopold, M.D.)

19 March 1953

BILATERIAL METASTATIC CARCINOMA OF UVEAL TRACT WITH ORBITAL EXTENSION. Carroll R. Mullen, M.D., Perce DeLong, M.D., and Charles G. Steinmetz, 3d*, M.D.

RE-EVALUATION OF BETA RADIATION THERAPY AND PRELIMINARY RESULTS OF STRONTIUM^{90} APPLICATOR. William F. Hughes, jr*, M.D.

16 April 1953

ACUTE HYPOTONY. P. Robb McDonald, M.D.

CYCLODIATHERMY (1 YEAR FOLLOW-UP OF 37 EYES). Bernard Lachman*, M.D.

RETROLENTAL FIBROPLASIA AND ITS RELATIONSHIP TO OXYGEN. Robert Bedrossian*, M.D. (Discusser: William O. LaMotte, jr, M.D.)

CHRONIC, PROGRESSIVE, EXTERNAL OPHTHALMOPLEGIA—A CLINICAL AND NEUROPATHOLOGICAL REPORT. Gabriel A. Schwarz, M.D., and Chan-Noa Liu*, PH.D. (Discusser: Francis Heed Adler, M.D.)

SECTION ON OTOLARYNGOLOGY[4]

21 January 1953

ADVANCES IN BRONCHO-ESOPHAGOLOGY

ESOPHAGOLOGY. Gabriel Tucker, M.D., Joseph P. Atkins, M.D., and William A. Lell, M.D.

BRONCHOLOGY. Chevalier L. Jackson, M.D.

DIAGNOSIS AND TREATMENT OF BRONCHIAL NEOPLASMS. Louis H. Clerf, M.D.

18 February 1953

SURGERY OF THE FACIAL NERVE. Frank D. Lathrop*, M.D. (Discusser: Robert A. Groff, M.D.)

18 March 1953

(Joint meeting, in New York, with the Section on Otolaryngology of the New York Academy of Medicine.)

15 April 1953

LATERAL SINUS—ANATOMIC VARIATIONS. I. Richard Adelizzi, M.D. (Discusser: Matthew S. Ersner, M.D.)

[1] Published in this (August, 1953) issue of the *Transactions & Studies.*

[2] Published in the June, 1953, issue of the *Transactions & Studies.*

[3] Abstracts of the presentations at this Section customarily appear in the *American Journal of Ophthalmology* and the *A. M. A. Archives of Ophthalmology.*

[4] Abstracts of the presentations at this Section customarily appear in the *A. M. A. Archives of Otolaryngology.*

† Quart. Bull. Coll. Va., vol. 51, no. 4, p. 11, July, 1954

Tracheotomy in Tetanus. Louis K. Elfman, M.D., Thomas A. Haymond*, M.D., and Wallace L. Chambers*, M.D. (Discusser: Floyd J. Putney, M.D.)

Otolaryngologic Investigation of a Penicillin Derivative with Unusual Properties. Louis E. Silcox, M.D. (Discusser: Harrison F. Flippen, M.D.)

SECTION ON PUBLIC HEALTH, PREVENTIVE AND INDUSTRIAL MEDICINE

27 April 1953

The World's Health Is Our Problem
Dr. Edward Krohn, Norway: Moderator

Post-war Health Problems in Western Germany. Dr. Hildegarde Rothmund.

Population Pressures in India Associated with Public Health Achievements. Dr. M. Shama Rao.

Chile's Major Public Health Problems. Dr. Rolando Armijo.

The Realities Confronting Korean Public Health: Reflections on the Need for Integrating Programs of Medical Assistance. Dr. C. C. Lee.

Major Communicable Disease Problems of Brazil with Emphasis on Schistosomiasis and Chaga's Disease. Dr. Louis Lima.

Abstracts

Abstract 1

Nickel Poisoning with Particular Respect to Nickel Carbonyl. F. William Sunderman, M.D., and J. F. Kincaid, PH.D.

In anticipation of the increased industrial use of nickel carbonyl, an investigation of its hazards was undertaken. The LD_{50} for acute exposure was determined for mice, rats and cats. The values for each of these species after thirty-minute exposures were 0.067, 0.24 and 1.9 mg./l respectively. These findings suggest that the values for the LD_{50} are directly proportional to the $\frac{2}{3}$ power of the body masses of the three species studied. Studies of subacute toxicity indicated that the material was not cumulative over a period of a few weeks and that tolerances developed following exposures to sub-lethal concentrations. Administration of British Anti-Lewisite to rats exposed to nickel carbonyl increased their tolerance to nickel carbonyl by a factor of 2. In human subjects exposed to nickel carbonyl the amount of nickel excreted in urine is increased above the normal.

Abstract 2

Diffuse Collagen Disease Complicating Malignancy. John Lansbury, M.D.

Over a period of 7 years, the author has collected 4 cases of "collagen disease" (namely rheumatoid arthritis, dermatomyositis and disseminated lupus erythematosus) which arose in patients suffering from the following types of malignancy: carcinoma of the esophagus, Krukenberg tumor of colon, carcinoma of the kidney, and malignant seminoma of the testes. In all instances the neoplasm preceded the collagen disease, although the presenting symptom in 3 of the 4 cases was "arthritis" and the malignancy was at first unsuspected. All four patients were of an allergic diathesis although their allergies were clinically unimportant.

A review of the literature discloses reports of the co-existence of dermatomyositis with a variety of unrelated neoplasms in about 30 instances. In 10 such cases the dermatomyositis subsided when the neoplasm was removed. Polley *et al.* reported 4 instances of arthritis complicating localized fibrous mesothelioma of the pleura with disappearance of the articular manifestations in 3 or 4 cases when the neoplasm was resected.

From the foregoing we can conclude that a relationship exists between neoplasia and "collagen" (connective tissue) disease. Although uncommon, it is sufficiently definite to formulate this rule: "When arthritis or any one of the collagen diseases begins without preceding stress (infection, fatigue, emotional upset, etc.), a careful search for hidden malignancy should be undertaken".

Abstract 3

THE CLINICAL VALUE OF TESTS FOR KETONEMIA IN THE DIAGNOSIS OF AND TREATMENT FOR DIABETIC COMA. Garfield G. Duncan, M.D., and Kenneth R. Knox, M.D.

Introduction

The mortality from diabetic coma varies from approximately 1 to over 50 per cent in reputable hospitals. The important aims in attempts to reduce the mortality are: early diagnosis, early treatment, adequate amounts of insulin at the outset of therapy, and appropriate tapering off of the amounts of insulin given as the ketosis regresses.

Early Diagnosis and Treatment

Early diagnosis is possible by simply finding grade 4 positive qualitative tests for glycosuria and ketonemia in the subject with clinical evidences of ketosis. *Initial* therapy with insulin and salty broth is started at once—in the home and the patient then is removed to a hospital.

Degree of Ketosis

Grade 4 reactions for ketones in undiluted plasma but less than grade 4 reactions in plasma which is diluted 1:1 with normal saline indicate a mild ketosis which will respond readily to relatively small amounts of insulin. Whereas if, in addition to a grade 4 reaction in the undiluted plasma, similar reactions are obtained in the plasma diluted 1:1 with normal saline and in the further or second dilution 1:1 with normal saline, the ketosis is of profound degree and a large initial dose—as much as 300 units—of regular insulin is indicated.

Subsiding Ketosis

As the ketosis subsides, the sensitivity to insulin returns. This returning sensitivity to insulin is detected most readily by the reduction in the degree of ketonemia noted first in the diluted and finally in the undiluted plasma. Suitable reductions in the amounts of insulin administered and appropriate prolongation of the intervals between the injections indicated by these findings should eliminate the danger of hypoglycemic reactions in the early post-ketotic phase.

Conclusion

Simple qualitative and crudely quantitative tests for ketones in the blood plasma have made it possible to (a) confirm the diagnosis of diabetic coma at the bedside—in the home and (b) permit earlier therapy than would otherwise be the case. Furthermore, these tests permit (c) an accurate appraisal of the degree of ketonemia and (d) provide an indication for the initial amounts of insulin to be given. Also (e) the subsiding ketonemia and the parallel returning sensitivity to insulin are detected by these tests hence providing an important indication for the reduction in the amounts and increased dispersal of the insulin therapy.

Abstract 4

THE INCIDENCE OF ENDOCRINE DYSFUNCTION FOLLOWING POSTPARTUM HEMORRHAGE AND/OR SHOCK. Norman G. Schneeberg, M.D., William H. Perloff, M.D., and S. Leon Israel, M.D.

Seventeen women who survived postpartum hemorrhage and/or shock were subjected to an endocrinologic survey because of the known relationship between such postpartum complications and the subsequent development of pituitary insufficiency (Sheehan's Syndrome). The study was particularly designed to reveal examples of masked or latent Sheehan's Syndrome. Three of the seventeen patients showed definite evidence of hypopituitarism. Of the remaining fourteen cases, four exhibited certain clinical symptoms and signs and borderline or abnormal laboratory findings insufficient to make a definite endocrine diagnosis but of sufficient magnitude to consider these patients subjects for continued observation and study. No correlation was found between the severity of hemorrhage and shock and evidence of endocrinopathy. The negative findings in certain patients with profound prolonged shock may be ascribed to 1) the need for further study and observation since Sheehan's Syn-

drome may appear after a latent period of months or even years; 2) insensitivity of available laboratory tests; 3) the lack of a true cause-and-effect relationship between postpartum hemorrhage/shock and pituitary necrosis. Further study of these patients and of additional subjects may yield the necessary information.

Abstract 5

GASTROINTESTINAL PRESSURE RECORDINGS IN MAN: PRELIMINARY REPORT ON PHYSIOLOGICAL AND PHARMACOLOGICAL ASPECTS. Stanley H. Lorber, M.D. and Harry Shay, M.D.

Intraluminal gastro-duodenal pressures were measured in 48 patients employing a Sanborn Poly-Viso recorder to amplify pressures transmitted through strain gauges from open-lumened tubes. Number ten French, single-lumen tubes with radio-opaque, whistle-tipped ends were found to be most satisfactory although tubes with lumina as small as the quadruple-lumened Miller-Abbott tube transmitted pressure accurately but with a slower rate of response to pressure change. To maintain patency of the tubes, saline was infused through them by motor driven syringes at rates of 2 cc. per hour.

Gastric pressures were observed to vary with changes in position of the subject being 2 to 2½ times higher in the sitting and standing positions as compared to that in the recumbent position. The pressure from fundus to antrum varied little if at all with the patient recumbent, but in the sitting and standing positions a gradient from antrum (18 cm. water pressure) to fundus (15 cm.) was observed. The positive gradient from antrum to duodenal cap area also increased when the subject was standing or sitting as compared to the recumbent position. Ingestion of an 8 ounce barium meal or insufflation of stomach with 300–500 cc. of air increased the baseline of intragastric pressure. Transport to the duodenum occurred in association with small and large pressure waves. Studies have been made on a new antispasmodic Bentyl Dihydrochloride[5], which when administered intramuscularly either decreased the height of pressure waves or suppressed them completely depending upon the dosage employed.

Abstract 6

THE DETECTION OF PRE-CLINICAL CARCINOMA OF THE LUNG ON ROUTINE CHEST X-RAY. Katharine R. Boucot, M.D., and Martin J. Sokoloff, M.D.

Little accurate information is available regarding the prevalence of bronchogenic carcinoma. The United States death rate per 100,000 population increased from 1.1 in 1920 to 11.3 in 1948. The need for intensified case-finding efforts is apparent but there is doubt as to whether or not mass chest x-rays constitute an appropriate technique. Despite over-reading of photo-fluorograms as "suspect neoplasm" and referral of individuals with such survey readings as emergencies, only 15 of 74 consecutive proven cases of bronchogenic carcinoma are alive 2 months to 6 years after the first abnormal film. Of the 15 survivors only 8 have been resected. Therefore, long term survival is only possible for 10 per cent.

The composition of the 74 patients was as follows: 51 white, 21 Negro, and 2 oriental. The ratio of males to females was 9:1. All 7 females were white and all have died.

The over-all rate of resectability was 30 per cent. Resectability rates increased with increasing age.

The lesions noted in the first available films read as abnormal were masses in 28 instances, infiltrations in 30 instances, excavations in 5 cases, and, in decreasing order of frequency, atelectasis, pneumonic consolidation, hilar prominence, fluid and obstructive emphysema. Twenty-two individuals had "negative" chest films available prior to their abnormal photofluorograms. On retrospective review 11 of

[5] Bentyl Hydrochloride is the trade-mark of The Wm. S. Merrell Company, Cincinnati 15, Ohio, for its brand of Dicyclomine Hydrochloride (diethylaminocarbethoxybicyclohexyl hydrochloride).

these had been erroneously interpreted as negative.

Five men had both active tuberculosis with positive sputum and bronchogenic carcinoma.

Twenty-six of the 74 patients had had symptoms of sufficient severity to warrant consultation with a physician but, on careful questioning, only 7 were truly asymptomatic. Three of the 7 men without symptoms were resected and are still alive. There was no significant difference in symptomatology between the two symptomatic groups—those 26 who had consulted physicians and the 41 who had not.

It appears that, if mass x-ray surveys have a real place in case-finding for bronchogenic carcinoma, it is among truly asymptomatic individuals. The lay public, particularly men over 45, should be encouraged to report regularly for survey films when in robust health but to their doctors in the presence of cough, weight loss, chest pain or blood-streaking.

There is urgent need for further investigation of the value of serial films and particularly of the optimal interval for retakes.

Abstract 7

Diffuse Interstitial Fibrosing Pneumonitis. J. J. Kirshner, M.D.

A case report of a patient in whom lung biopsy revealed a diagnosis of chronic interstitial fibrosing pneumonitis. This was later confirmed by autopsy studies. Fifteen previous cases were found in the American literature, all being diagnosed by post mortem study. The etiology of the condition is obscure. The clinical features are respiratory insufficiency leading to cor pulmonale and death. There is no indication from the history, clinical course, laboratory or histological studies of a bacterial infection or chemical irritation that might be responsible. Hamman in his original report suggested a virus etiology. The histological features are a diffuse interstitial fibrosis with extensive proliferation of connective tissue within the alveolar walls. The condition appears to represent a distinct clinico-pathological syndrome that if inflammatory may well represent a type of tissue response to some unknown virus.

Abstract 8

Coincident Hypertension and Addison's Disease. Alexander Margolies, M.D., Henry M. Wise, M.D., and William A. Jeffers, M.D.

The coexistence of hypertension and Addison's disease is rare, but has been reported by those interested in endocrine factors in relation to blood pressure. Thorn and Perera have described the return of blood pressure to hypertensive levels when adrenal insufficiency was corrected in 6 patients who exhibited this particular combination of diseases.

The patient to be described in this report was referred to one of us (WAJ) because he had been found to have postural (orthostatic) hypotension. That the postural fall in blood pressure was related to Addison's disease was not appreciated until the behavior of several hypertensive patients subjected to extensive adrenal resections had been observed. Following adrenalectomy in the case of severe *hypertension*, the reappearance of postural *hypotension*, once the blood pressure has become stabilized, may herald the onset of adrenal insufficiency.

Subsequently, with the use of sodium chloride and desoxycorticosterone acetate (DCA), our patient's blood pressure has become stabilized in a mildly hypertensive range. The tendency for his blood pressure to fall during quiet standing is no longer present.

Abstract 9

The Problem of Gross Gastrointestinal Bleeding. Paul Cimoch, M.D., Herbert A. Yantes, M.D., and C. Wilmer Wirts, M.D.

The purpose of this report is to present an analysis of our findings in the diagnosis and treatment of 232 patients admitted to The Jefferson Medical College and Hospital with gross gastrointestinal bleeding over a period of three years from 1950 to 1953. The data is based on two groups of patients; the former consists of 120 patients who were individually

managed by the attending physicians who happened to be on service on the respective medical wards to which the patient was admitted and the latter, 112 patients, regularly observed by a team with representatives from the medical, surgical, clinical laboratory and radiologic services who recommended management.

As a result of our experience in the two methods of management of these patients we are convinced that the team management offers superior care to the patient in comparison to individual management. We believe this to be so because we know there is a significant number of patients, particularly those with massive bleeding who will require operation as a life-saving measure. It seems logical to expect increased efficiency when representatives from each of the services involved have become accustomed to working together and discussing the mutual problems presented by these patients. To overcome the defects that appeared to exist in the individual management of these patients we now consider any patient over 50 years of age admitted with massive bleeding or who has recurrent bleeding after admission a surgical candidate unless a contraindication to surgery is demonstrable by virtue of associated disease. One of the most formidable contraindications to operating on these patients is the presence of portal cirrhosis with the possibility of bleeding from esophageal varices. In this regard we have found the bromsulphthalein test of such effective aid that we use it now routinely as an aid in differential diagnosis. If esophageal varices and blood dyscrasias are excluded as the cause of bleeding it leaves few patients in whom surgical management is not feasible.

Abstract 10

THYROID FUNCTION AS REVEALED BY NEW RADIOACTIVE IODINE TECHNICS. Robert Robbins, M.D.

The biochemical aspects of thyroid physiology is reviewed, with particular reference to the steps involved in the synthesis and use of the thyroid hormone. The commonly used tests of thyroid function, the BMR, the protein bound iodine determination and the radioactive iodine uptake studies are related to this schema.

The rates of the various aspects of the synthesis of the hormones is discussed, as demonstrated by radioactive iodine technics. For example, it is shown that the thyroid gland removes radioactive iodine from the plasma at a rate of approximately six or seven per cent per hour, and the kidney removes it at a rate of approximately eight or nine per cent per hour so that the radioactive iodine disappears from the plasma at a total rate of approximately fifteen per cent per hour. This leads to the concept that the "average life", or turnover time of radioactive iodine in the plasma is approximately seven hours in the euthyroid patient. In the thyrotoxic patient this may be reduced to as short an interval as one-half hour to one hour. This avidity of the thyroid for radioactive iodine is also demonstrated, although less precisely, by simpler measures of the iodine collecting function of the gland, such as the twenty-four hour uptake or the twenty-four hour urinary excretion. Some of the disadvantages of the latter studies are touched upon.

It is also possible to study the rate at which radioactive iodine is incorporated into the thyroid hormone itself and the rate at which this radioactive thyroid hormone is released from the thyroid gland. In normal patients this is released at a rate so as to correspond with an average life or turnover time of approximately two weeks in the normal patient. In thyrotoxicosis, the release is accomplished at an average life or turnover time of approximately three to five days.

In a similar fashion there is shown the length of time over which the thyroid hormone exists in the circulating blood after it has been released; that is, we can evaluate the rate at which thyroid hormone is utilized. This can be approached from two directions, and both experimental procedures give essentially the same results, namely that thyroxin exists in the body for an average life or turnover time of approximately three to five days in the euthyroid

patient, and approximately one to two days in the thyrotoxic patient.

The possible future usefulness of the organic iodine studies in diagnosis is touched upon.

Abstract 11

MITRAL COMMISSUROTOMY IN THE OLDER AGED PATIENT. O. Henry Janton, M.D., Robert P. Glover, M.D., and Thomas J. E. O'Neill, M.D.

An analysis of twenty consecutive cases of mitral stenosis (from a total of 350 cases), aged fifty to sixty-one, treated by commissurotomy from May 1951 to October 1952 is presented.

A history of rheumatic infection was obtained in eight. Three had recurrent hemoptyses and five had had one or more systemic emboli. Eighteen had congestive heart failure controlled before surgery in all but three. Eleven had pure mitral stenosis and in another eight an associated mitral insufficiency was present. One had predominant mitral stenosis with associated mitral and aortic insufficiency.

That patients in this age group can and do tolerate intracardiac surgery is evidenced by the fact that there was no operative mortality. In fifteen there has been definite functional improvement. Three have been unimproved and two have died, six months and one year after surgery.

This series would indicate that the patient over fifty with symptomatic mitral stenosis can have a functionally satisfactory commissurotomy performed without undue operative risk and with essentially the same ultimate degree of improvement enjoyed by patients requiring treatment at an earlier age.

Abstract 12

THE USE OF SODIUM DEHYDROCHOLATE IN THE DIAGNOSIS OF BILIARY TRACT DISEASE. Joseph M. Gambescia, M.D., Charles M. Thompson, M.D., Alex Ulin, M.D., and William Shoemaker, M.D.

Sodium dehydrocholate administered intravenously produces a measurable response in both normal and abnormal states. In this study, comparison of duodenal aspirates as to volume and icterus index for three 20 minute intervals before and after the intravenous injection of 10 cc. of 20% sodium dehydrocholate indicates that a difference in response occurs under the following situations: 1) the normal gall bladder; 2) cholecystolithiasis (with or without impaired roentgen function); 3) choledocholithiasis; 4) post cholecystectomy.

This preliminary report entails the study of 7 normal and 52 abnormal situations and in essence supports the work of Lans, Stein, and Meyer (*Gastroenterology* **18:** 64, 1951).

The normal response comprises a fall in both volume and icterus index of the duodenal aspirate after the I.V. injection of sodium dehydrocholate apparently due to the diversion of the increased hepatic secretion into the gall bladder (reservoir function).

The abnormal response comprises a rise in volume and a decrease in icterus index following the intravenous administration of sodium dehydrocholate—a reflection of the inability of the gall bladder to accommodate the increased flow of hepatic secretion (no reservoir function) and an indication of the hydrocholeretic effect of sodium dehydrocholate (an increase output of secretion comparatively lower in pigment content).

Illustrative cases will be considered demonstrating the above mentioned categories.

Further study is necessary for proper definition of this test, but at present, indications are that it will be of value in aiding to evaluate: a) the normal gall bladder; b) the abnormal gall bladder with normal concentrating function (cholecystography); c) post cholecystectomy syndrome; d) the jaundiced patient in whom it is not possible to visualize the gall bladder by X-ray and in whom the problem of biliary tract disease arises as a contributing cause to the jaundice.

Abstract 13

SERUM ELECTROLYTES IN UREMIA. F. William Sunderman, M.D.

Measurements of electrolytes and non-electrolytes have been made in the sera obtained from

patients in the terminal stages of uremia. These data were considered in relation to the total osmotic pressures as determined by freezing point. Our studies support the view that in renal insufficiency with uremia, one of the most important functions of the kidney has been lost—namely, the maintenance of normal osmotic pressure relationships. It appears that the critical upper levels of total osmotic pressure beyond which changes in the human protoplasmic structure are irreversible, correspond to freezing point depressions between 0.65° and 0.70°C.

Abstract 14

TOTAL THYROID GLAND TRANSPLANT USING VASCULAR ANASTOMOSES IN TREATMENT OF CHRONIC TETANY. Julian A. Sterling, M.D., and Ralph Goldsmith, M.D.

The case is a report of a 28 year old woman. In 1942 the patient had a thyroidectomy. Following this she had hypothyroidism, hypoparathyroidism and laryngeal stridor due to cutting of both recurrent laryngeal nerves. The larynx was rehabilitated by the surgical fixation of a vocal cord. She was given all the usual medication for the glandular deficiencies. In 1952 she was taking five to six grains of thyroid extract, at least 120 grains of a calcium compound and three to four cc. of AT 10 daily. Nonetheless, attacks of tetany occurred with increasing frequency. In 1949, parathyroid gland was obtained at time of thyroidectomy in a 40 year old patient and transplanted to the patient using the "tissue culture" technique. This transplant failed.

By the summer of 1952 the patient was reporting to the accident room of the Albert Einstein Medical Center three to four times a day to receive 30 to 40 cc. of calcium gluconate intravenously each time to overcome tetany. No other medication would relieve it.

It was thought that the most active parathyroid tissue was present in the infant and child. Since the glands are so tiny, it was conceived that all useful parathyroid tissue could be procured by removing the entire thyroid gland. In addition, it was thought to preserve the blood supply by removing vascular pedicles with the thyroid gland. Accordingly, the thyroid gland together with the carotid arteries and jugular veins bilaterally were removed from the body of a recently deceased infant and vascular anastomoses completed in the inguinal canal of the patient to accomplish the transplant.

Since operation, the patient has taken neither thyroid extract nor AT 10. Weight is unchanged, BMR is normal, chemistries are normal and there is no tetany. Thus far, only five months has elapsed. Even if the transplanted gland should fail to function in the future, it has been demonstrated that the new method reported here is feasible.

Abstract 15

THE EFFECT OF GANGLION BLOCKING AGENTS IN CONGESTIVE HEART FAILURE. Charles R. Shuman, M.D., Norman Learner, M.D., and John N. Doane, jr., M.D.

Intravenous administration of tetraethyl ammonium (150 to 500 mg.) and hexamethonium (12.5 to 50 mg.) was conducted in a group of 21 patients with congestive heart failure. The types of underlying cardiac disease included hypertensive, arteriosclerotic, mitral stenosis and scoliotic. The effects upon venous pressure, arterial pressure, pulse rate, skin temperature and digit plethysmographic readings, vital capacity and the degrees of dyspnea and orthopnea were recorded. Similar data were obtained in a group of seven patients in whom cardiac disease was absent. The venous pressure in the congestive failure patients fell from a mean of 174.5 to 85.0 mm. saline; the mean vital capacity rose from 1620 cc. to 2122 cc. after administration of these agents. The skin temperature and digital plethysmograph readings gave evidence of an increased blood flow in these areas in the non-failure patients. However, in patients with congestive failure only two of the 11 in whom these data were obtained showed a rise in cutaneous or digital blood flow. Amelioration of the symptoms due to pulmonary congestion, dyspnea and orthopnea, was evidenced to varying degrees in the

congestive failure group. Some of these patients were markedly improved. The failure to observe an increase in cutaneous blood flow in the feet and hands in the heart failure patients suggests that the principal action of these drugs was manifested in other areas of increased vascular tone to account for the reduction of venous and arterial pressures. The clinical improvement manifested in this group is probably due to redistribution of the blood volume to regions peripheral to the cardiopulmonary and central venous circuits.

Pathological Society of Philadelphia

PROCEEDINGS
N. S. Vol. 41: OCTOBER, 1952–MAY, 1953
Clark E. Brown, *President*
Warner F. Sheldon, *Secretary*

October 9, 1952

CARCINOMA IN SITU

REPORT OF THE PHILADELPHIA COMMITTEE FOR THE STUDY OF CERVICAL CARCINOMA IN SITU. Ernest E. Aegerter. (*Abstract 1, below*)

REVIEW OF THE LITERATURE ON THE FOLLOWED CASES. A. Valdes-Dapena. (No abstract supplied.)

THE HISTOLOGIC DIAGNOSIS. Henry Brody. (*Abstract 2, below*).

THE CYTOLOGIC DIAGNOSIS. John F. Seybolt. (*Abstract 3, below*).

November 13, 1952

AWARD OF THE WILLIAM WOOD GERHARD MEDAL

"CORRELATIONS OF STRUCTURE AND FUNCTION AND MECHANISM OF RECOVERY IN ACUTE RENAL FAILURE". Jean Oliver. (No abstract supplied).

December 11, 1952

SYMPOSIUM ON THE ADRENAL GLANDS

CLINICAL ASPECTS. George Strong. (No abstract supplied).

ENDOCRINOLOGICAL ASPECTS. Joseph Rupp. (*Abstract 4, below*).

PATHOLOGY. Marshall Lieber. (No abstract supplied).

January 8, 1953

GENETIC FACTORS IN TISSUE RESPONSE TO INJURY

INTRODUCTION. John E. Gregory. (*Abstract 5, below*).

IN EXPERIMENTAL TUBERCULOSIS. Max B. Lurie, Peter Zappasodi, Arthur M. Dannenberg, Jr. and George H. Weiss. (*Abstract 6, below*).

February 12, 1953

SOME FACTORS INFLUENCING METASTASIS OF TUMORS IN MICE. Thomas C. Pomeroy. (*Abstract 7, below*).

POPULATION STUDIES ON ASCITES TUMORS. Theodore S. Hauschka. (*Abstract 8, below*).

THE MYOEPITHELIUM OF THE HUMAN BREAST. Helen Ingleby. (*Abstract 9, below*).

March 12, 1953

Annual Joint Meeting with Section on Clinical Pathology of the Philadelphia County Medical Society.

May 14, 1953

SLIDE SEMINAR

PROBLEMS IN THE DIAGNOSIS OF LYMPH NODES. R. Philip Custer.

ABSTRACTS

Abstract 1

REPORT OF THE PHILADELPHIA COMMITTEE FOR THE STUDY OF CERVICAL CARCINOMA IN SITU. Ernest E. Aegerter.

At the request of the Philadelphia Committee for the Control of Cancer, a committee composed of the directors of 13 laboratories in the Philadelphia area was appointed to investigate the incidence, prognosis and criteria for diagnosis of carcinoma in situ of the female cervix. Each member submitted material on 3 types of cases, one of what they considered classical carcinoma in situ, one of typical metaplasia or epidermization and one case which he felt was equivocal. Slides were made and sent out as

unknowns to each committee member. Accompanying the slides was a form sheet asking certain information pertinent to the diagnosis of carcinoma in situ as made in the clinic of that particular pathologist. The following is an analysis of the data:

The total number of cervices examined in the 13 institutions in the 3 year period was 15,124. There were 994 cases (6.5%) of primary carcinoma of the cervix. Included in this number the diagnosis of carcinoma in situ had been made 86 times thus establishing an incidence of approximately 8.6%. During this period the diagnosis of "atypism, pre-malignant or suspicious" was made 68 times with a relationship of 6.8%. Four of these cases were eventually proven to be cancer. The diagnosis of carcinoma in situ was made four times in pregnant cervices. Forty cervices with the diagnosis of carcinoma in situ were removed and studied by pseudoserial section. Six of these were found to be frankly invasive carcinoma by this method.

One hospital with a predominantly Jewish clientele was polled. Its cervical cancer incidence was 2.7% in contrast to an average of 9.7%. The variation in diagnosis was not as wide as might be expected. There was universal agreement on several cases of carcinoma in situ. All of these had loss of the maturation pattern. The widest variance in opinion came in those cases in which there was basilar hyperplasia and a retaining of superficial maturation. When the curve of age incidence of carcinoma in situ was superimposed upon that of frank carcinoma of the cervix it was found that the two curves paralleled each other, the former being about 10 years earlier.

Abstract 2

Cervical Carcinoma in Situ: The Histological Diagnosis. Henry Brody.

In 1939 Robert Meyer (Surg., Gynec. & Obst. **73:** 129, 1941) said: "Experience has taught that early histological changes may now be recognized which will certainly lead on to a fatal issue in the absence of treatment. This was at the beginning, and still is, the definition of the malignancy of the tumors we call cancer." The diagnoses of cervical carcinoma-in-situ are still not based on uniform criteria, and individual cases are being variously diagnosed in different laboratories. To set down acceptable criteria for diagnosis is not as difficult as it might seem. The problem is not a new one, though the last decade has seen a reawakening of interest. In 1910 Rubin (Am. J. Obst. **62:** 668, 1910) set down criteria for "incipient carcinoma" which are still useful. These were based on cellular and nuclear atypism and on loss of the normal maturation pattern. Difficulties arise, at both ends of the scale, when one attempts to put such criteria into practice. When are anaplastic changes sufficient to warrant a diagnosis of carcinoma? How much atypism may be found in the healing erosion? Are the bizarre cells and atypical mitotic figures associated with severe inflammation capable of regression? At the other end of the scale, what constitutes invasion? Does growth into the mouth of a cervical gland constitute invasion, or must there be clear evidence of a break through a basement membrane? How is the latter to be recognized? These problems were illustrated with a series of lantern slides. Definitive answers are still difficult. Only prolonged follow-up of well studied cases will bring us to the time when subjective factors will not negate Robert Meyer's optimistic dictum.

Abstract 3

Cervical Carcinoma in Situ: The Cytologic Diagnosis. John F. Seybolt.

The abnormal cellular pattern found in vaginal smears and which corresponds to the pathological diagnosis of carcinoma in situ of the cervix has been called by Dr. Papanicolaou "dyskaryosis". He recognizes four types of dyskaryosis: superficial cell, intermediate or navicular cell, parabasal cell and endocervical cell dyskaryosis, depending upon the predominate cell type involved. The term itself (dyskaryosis) implies that the principal morphological changes pertain to the nuclei, and the criteria used in identifying this cellular

pattern are: nuclear enlargement, hyperchromasia, irregularity in nuclear form, multinucleation, and peri-nuclear vacuolization. This last criterion is especially apparent in the superficial cell type. These changes need not be present all in one cell, but they are usually found among cells in a group or in various cells scattered throughout the smears. The cell type is usually quite apparent because of minimal morphological changes in the cytoplasm. The clinical significance of the various types of dyskaryosis is unknown.

Several methods of collecting satisfactory specimens have been used. The cervical scraping, performed either with a cotton-tipped applicator or an Ayre wooden spatula, as well as an aspirate of the cervical canal are the methods of choice since more cells are obtained with these technics than with the aspirate collected from the posterior fornix.

Unfortunately, there are other pathological conditions which may produce morphological changes leading to confusion in the interpretation of the smears. The principal ones are: pregnancy, trichomonas infestation, and bacterial infection. In addition, there have been reports from various laboratories that estrogenic therapy, irradiation, and condyloma acuminatum may also cause confusion. We believe that strict adherence to the criteria as outlined above will diminish the chance of errors in interpretation.

The problem of spontaneous reversibility of the dyskaryotic pattern has been encountered in several instances. It is difficult to explain such a phenomenon, for most pathologists do not consider carcinoma as ever being a self-eradicating lesion. It has been suggested that natural desquamation might account for the reversibility, but this is highly speculative.

Abstract 4

ADRENALS: ENDOCRINOLOGICAL ASPECTS. Joseph J. Rupp.

The steroids secreted by the adrenal cortex may be classified physiologically into three main groups: (1) the 11-desoxycorticoids, produced in the zona glomerulosa, regulate electrolyte metabolism, (2) The C-11-oxysteroids, produced in the zona fasciculata, have many actions, among which are protein catabolic and gluconeogenic actions, (3) The androgenic 17-ketosteroids, which are produced in the inner zona fasciculata and the zona reticularis. The rate of production of the steroids is controlled by the levels of adrenocorticotrophin. Inhibition of adrenocorticotrophin formation, as by exogenous cortisone or hydrocortisone causes atrophy and hypofunction of the adrenal cortex.

Hyperfunction of the adrenal cortex may be associated with tumor, hyperplasia, or no histologic alteration of the adrenal cortex. The types of syndromes produced by adrenal hyperfunction will depend on the nature of the steroids produced in excessive amounts. In Cushing's Syndrome all of the steroids are produced in excess. The virilization in the adrenogenital syndrome is the result of the excessive androgenic 17-ketosteroids. Female pseudohermaphroditism or macrogenitosomia precox in the male is associated with hyperplasia of the adrenals which begins in utero. Some patients with congenital androgenic hypercorticalism have the electrolyte imbalance typical of Addison's Disease, and may develop crisis because of the lack of 11-desoxysteroids, or perhaps the production of a salt losing adrenal hormone.

Abstract 5

GENETIC FACTORS IN TISSUE RESPONSE TO INJURY: INTRODUCTION. John E. Gregory.

There is today a marked swing in the interest of many investigators away from specific etiologic agents and toward host factors in the etiology and pathogenesis of disease.

One such host factor or group of factors are those which depend upon genetic variations. There are at least two types of variations, those which are directly responsible for disease, as are seen in hemophilia, sickle-cell anemia and Huntington's chorea, and those which render an individual, or a race, more susceptible to more or less well defined causative agents. Ex-

amples of such diseases are cancer, rheumatic fever and tuberculosis.

To recognize, or even to sharply define, the genetic factor in these diseases is obviously only a partial answer to the etiologic problem. One wants to know *why* certain races of people or animals are highly susceptible to tuberculosis, for instance, and others highly resistant. The possible answers to such a question are numerous. For example, the chemical composition of the "target" tissues may vary; the level of reticulo-endothelial activity may vary in several respects and this in turn may be influenced by several possible mechanisms. It takes courage of the highest order to attack such a problem. We have, here in Philadelphia, a man who has such courage, a man who for a number of years has been engaged in trying to find out why certain races of rabbits are susceptible to tuberculosis and others are highly resistant. I refer to Dr. Max Lurie of the Phipps Institute.

Abstract 6

Genetic Factors in Experimental Tuberculosis. Max B. Lurie, Peter Zappasodi, Arthur M. Dannenberg, Jr. and George H. Weiss.

An analysis of the pathogenesis of tuberculosis induced in inbred rabbit races of different genetic resistance to the disease by various methods of inoculation of bovine, human and attenuated tubercle bacilli has demonstrated that native resistance to tuberculosis in the rabbit is determined by the innate varying capacity of the phagocytes that ingest the micro-organism to inhibit their intracellular multiplication, initially, and by their varying inborn aptitudes to develop rapidly and effectively an increased power to destroy the micro-organism after the onset of the infection. The resistance acquired by a given race during the course of a given infection or after a certain immunization is greater in the natively resistant than in the natively susceptible strains.

High native resistance is often but not always associated with a low connective tissue permeability and, more commonly, with a high level of development of allergic sensitivity and antibodies. Estrogen, by reducing the connective tissue and vascular permeability, retards the dissemination of the disease and prolongs its course. Gonadotrophin enhances the spread of the disease and shortens its duration by increasing connective tissue and vascular permeability. Neither hormone influences the growth and destruction of tubercle bacilli in the tissues, antibody production or the essential nature of the development of allergic sensitivity.

There is an incomplete parallelism between native resistance and adrenocortical function as indicated by its mass in relation to body weight. Cortisone in pharmacologic doses reduces the innate capacity of the phagocytes to destroy the ingested bacilli. It suppresses nonspecific and allergic inflammation as a result of the protective effect exercised by the hormone on the capillary walls against agents which increase their permeability. Cortisone tends to localize the disease at the portal of entry temporarily because the hormone suppresses inflammation and consequently reduces the cellular and humoral bridges between the focus and the rest of the body. Withdrawal of the hormone reinstates the inflammation and the bacilli, accumulated in the foci during the cortisone treatment, now spread widely in the tissues and may cause a fatal issue in an animal which, without this, usually arrests the disease.

The most accurate, quantitative and rapid method of ascertaining native resistance thus far is that of exposing animals to the quantitative inhalation of human type tubercle bacilli, to which this species is relatively resistant, and of determining the number of grossly visible primary pulmonary tubercles generated in them 4 to 5 weeks after this infection. The greater the native resistance, the fewer are the tubercles formed after the inhalation of a given number of micro-organisms. Cortisone increases the number of foci produced in a given race by a given number of inhaled bacilli. Minimal doses of a certain preparation of sheep ACTH reduced the number of tubercles generated in rabbits with low adrenal function

but had no effect on a race with large adrenal cortices.

By this method, the determinants of native resistance were found to be multiple, complex and additive in nature. The resistance of the F_1 hybrids of a natively highly resistant and highly susceptible race was intermediate between that of each parent race. The back-cross of the F_1 hybrid generation to the resistant ancestors yielded a strain which was of the same degree of high resistance as the original resistant race. The back-cross of the F_1 hybrids to the susceptible ancestors was significantly more resistant than the original susceptible ancestors. Dominance of resistance over susceptibility is a possible, but not the only, interpretation of the observations.

Abstract 7

SOME FACTORS INFLUENCING METASTASIS OF TUMORS IN MICE. Thomas C. Pomeroy.

During the course of investigations on the effectiveness of various bacterial polysaccharides and the protective effect of cortisone and hydrocortisone on "metastatic" pulmonary tumors induced by intravenous injections of mammalian Ringer's suspensions of ascites tumor cells in Swiss mice, it was noted that widespread blood-borne metastases occurred with Krebs II adenocarcinoma and not with Sarcoma-37. This was found to be the result of the cortisone and hydrocortisone and not the effect of the bacterial polysaccharides. However both the polysaccharides and hydrocortisone increased the "takeability" of the Krebs II tumors in the lungs.

M. Agosin *et al.* (Proc. Soc. Exp. Biol. Med. **80:** 128, 1952) have noted a similar appearance of distant metastases of transplanted spontaneous breast adenocarcinoma in C3H mice concomitant with regression of the primary transplant while receiving large doses of cortisone. They concluded that metastasis was facilitated by breakdown of the barriers around the transplant by a hyaluronidase-like or hyaluronidase stimulatory action of cortisone.

This seemed contrary to the established effects of cortisone on the hyaluronidase system and also contrary to the evidence upholding the soil hypothesis of tumor metastasis. Further studies were designed to elicit the mechanisms involved by injecting ascites cell suspensions into the left ventricle of the heart. That the major if not sole effect of cortisone on this phenomenon was a lowering of "resistance" of the host tissue was demonstrated. Except for the ovaries and adrenals there was almost complete disparity between the development of many tumors in the cortisone treated animals and the absence of tumors in the same organs in the untreated animals. These findings were related to the observations of others on the effects of cortisone, ACTH and typical "stressors" on tumor transplantability and grafting of heterologous tissues in experimental animals through the mechanism of interference with the antigen-antibody reactions. The liver proved to be the critical organ for comparative study of this phenomenon. The marked variation in rates of growth in different organs was also well demonstrated and again illustrated a marked organ specificity for the tumor-host reaction in the phenomenon of metastasis as well for experimental direct transplantation of homologous and heterologous tumors into various organs. The high incidence of metastases in adrenals and ovaries of normal as well as cortisone treated mice is probably related to the high steroid content of these organs and this view is supported by the known effects of most steroids on lymphoid tissue.

These findings again emphasize that there is much more to the phenomenon of metastasis than the mere delivery of tumor cells or emboli to an organ and that the number of metastatic tumors that develop (though related to the mechanical factors which control the number of cells or emboli that arrive) are mainly determined by the local tumor-host reaction which is largely an antigen-antibody reaction. Further studies to clarify the local hormonal control of this reaction are in progress utilizing the above technique and will soon be expanded to include the single cell clones of identical chromosome population described in the following abstract by Dr. Hauschka in an effort to correlate the

antigenic variability of tumor cells with their varying ploidy.

Abstract 8

POPULATION STUDIES ON ASCITES TUMORS. Theodore S. Hauschka.

Twelve oncotypes, including several mouse carcinomas, sarcomas, and lymphomas, have been studied in the favorable ascites form. The cell populations were analyzed cytologically and immunogenetically with the following results: The neoplasms were shown (in collaboration with Dr. A. Levan) to fall into two sharply defined categories, modal values for chromosome number being either near diploid (40) or in the tetraploid region (80). An apparently constant correlation was established between chromosome constitution and antigenic specificity. None of the diploid tumors were able to grow progressively in hosts of foreign strains; but all the near-tetraploid ascites gave lethal takes in one or more foreign genotypes. This rule appeared to be independent of the tumors' origin, transplantation history, virulence and method of induction. For example, the diploid and tetraploid lymphomas #1 and #2, both induced in A-strain females by x-radiation with the same dosage, and carried through comparable numbers of serial passages in the A-strain, behaved as follows: Both tumors were 100% lethal in the home-strain. The tetraploid lymphoma #1 was easily "conditioned" to serial passage in the foreign DBA/2 strain, where it now causes a high percentage of deaths. The diploid lymphoma 2, although the more virulent, was nevertheless unable to grow in any of seven foreign genotypes tested, including DBA/2.

Without detracting in the least from the general validity of histocompatibility genetics, the influence of ploidy on host-range provides plausible chromosomal mechanisms for the phenomena of "antigenic simplification" and increased tissue specificity. Experiments now in progress are aimed at separating stock tumors into clonal sublines derived from single cells and differing in chromosome constitution, antigenicity, virulence and other features. The feasibility of this program is evident from successful isolation of such clones in the case of the Krebs 2 ascites carcinoma.

Abstract 9

THE MYOEPITHELIUM OF THE HUMAN BREAST. Helen Ingleby.

In spite of a fairly extensive literature mostly in German, French and Italian, the myoepithelium of the breast has received but scant attention in this country. K. C. Richardson (1949) has shown that its function is to expel milk from acini and ducts.

The myoid is most easily studied during pregnancy and in hyperplastic conditions. In early pregnancy clumps of basal cells are seen and their gradual transformation to epi- and myothelial cells may be followed. At ten days to two weeks gestation only the beginnings of differentiation are seen. At three weeks the nuclei of both types are similar but the myothelial cells show long, striated processes, while the epithelial cells tend to be arranged in rows. In the later stages of pregnancy similar clumps of embryonic cells are seen. The fibrils of the older myothelial cells arrange themselves around the acini and along the prelobular ducts.

Myoid hyperplasia occurs in many pathologic conditions. In adenosis the myoid may be continuous around the prelobular ducts and lobules. Sheaves of cells grow out and their fibrils merge with the intraductal tissue.

OFFICERS

President: Clark E. Brown (1952–53)
Vice-President: Mollie Geiss (1952–53)
Secretary: Warner F. Sheldon (1946–53)
Treasurer: Anthony L. Pietroluongo (1951–53)

Changes in Membership

New Members

	Date of Election		Date of election
Manuel Arthur Bergnes	10/ 9/52	Robert E. Bovard	12/11/52
René Lefebvre	10/ 9/52	Toby E. Silverstein	12/11/52
Masahiro Sakai	10/ 9/52	Richard Putnam	2/12/53
William Beautyman	10/ 9/52	Edward J. Benz	5/14/53
William C. Yakovac	10/ 9/52	Richard M. Shuffstall	5/14/53
Francis Beyer	10/ 9/52	Paul T. Carrigan	5/14/53
William Long	10/ 9/52	Geraldine Young	5/14/53
Dicran Y. Kassouny	10/ 9/52	Seymour Adelson	5/14/53
Henry L. Kazal	11/13/52	Bessie Dituri	5/14/53
Charles N. Wang	11/13/52	Margaret C. Collins	5/14/53
Jasper Chen See	11/13/52	Charles Q. Griffith	5/14/53
Newton L. Larkum	11/13/52	Stephen M. Hanson	5/14/53
William E. B. Hall	11/13/52	Anthony V. Torre	5/14/53
Khalil Al-Alousi	12/11/52	Rafael R. Ramirez Weiser	5/14/53

Resignations

Dr. William R. Platt (1952)

Deaths

Dr. Thomas R. Currie (1952)
Dr. G. M. Dorrance (1949)
Dr. Horace J. Forman, Jr. (1951)

William Wood Gerhard Gold Medal: Jean Oliver (1952)

TRANSACTIONS & STUDIES

of the

College of Physicians of Philadelphia

Volume 21 (Fourth Series)

Number 3 (February 1954)

The Present Status of Intracardiac Surgery for Mitral and Aortic Stenosis*

By ROBERT P. GLOVER†, M.D.

THE recent "Renaissance of Cardiac Surgery" has introduced new hope and assurance both to the medical profession and to the patient suffering from the cicatricial and disastrous end results of rheumatic fever. The demonstration in the past decade that the interior of the heart could be successfully invaded at will for the reconstruction of stenotic valvular disease inaugurated this new era of surgical achievement (1–3). Surgery, almost from its inception, has had as one of its primary objectives the relief of "obstruction and stricture" no matter where the offending block lay within the systems of the human body. It was logical, therefore, that with the application of basic surgical principles to cardiac disease initial attention and effort be directed toward the relief of "obstructed and strictured" valves.

Any consideration of valvular lesions, surgical or otherwise, must at once take into account the nature of their pathologic change. For reasons not entirely clear the valves within the heart predominantly undergo malformation according to their location within the vascular pump. Thus, the valves in the right heart (tricuspid and pulmonary) are primarily the seat of congenital deformities (4–5). On the other hand, the mitral and aortic valves in the left heart are damaged by superimposed acquired disease, usually rheumatic in origin. Whereas, prior to 1950, the congenital anomaly monopolized the surgeon's attention, today by far the greatest field of cardiac surgical endeavor is concerned with the problems of acquired disease. Already the stage of initial conjecture and speculation as to the proper application of newly devised intracardiac surgical techniques is passing. Experience to date has shown that surgical intervention at the proper time and in intelligently selected cases can be considered a major adjunct in the overall care of the rheumatic heart crippled by valvular stenosis (6–10).

Mitral Stenosis

In rheumatic disease the mitral valve develops numerous minute inflammatory verrucae in a row along the line of closure of the valve. With continuing rheumatic activity and attempts at healing over the course of

* Thomas Dent Mütter Lecture LXVI, College of Physicians of Philadelphia, 7 October 1953.

† Clinical Professor of Thoracic Surgery, Hahnemann Medical College, Philadelphia; Thoracic Surgeon to Episcopal, Presbyterian, and Lankenau Hospitals, and to St. Christopher's Hospital for Children, Philadelphia.

years there is a gradual development of fibrosis, thickening and narrowing of the valve leaflets as their cusp margins become adherent at the angles (commissures). This scarring may be limited in extent to resemble a purse-string puckering at the valve orifice with minimal involvement of the valve leaflets themselves, which remain quite pliable and of the consistency of kid glove skin. In other instances, the periorificial induration involves one-fourth to one-half of the valve cone leaving a correspondingly smaller margin of flexible tissue about the base at the A-V ring. In far advanced disease the whole valve may become rigid and completely inflexible—a hard, ovoid plaque surrounding a tiny fish-mouth slit. Calcium may be present at any stage as flecks, localized infiltration, or, rarely, almost completely replacing valve tissue. Thus, as stenosis is produced, pronounced resistance to the passage of blood from the left atrium into the left ventricle ensues. Since the egress of blood from the left atrium is impaired, increased pressure within and considerable dilatation of this chamber results. The high intra-auricular pressure is transmitted to the entire pulmonary vascular system and thence to the right side of the heart. A chronic pulmonary hypertension results with nocturnal or exertional pulmonary congestion (dyspnea), rupture of pulmonary capillaries (hemoptysis) and failure of the right side of the heart (hepatomegaly, ascites and peripheral edema).

Once this progressive pattern becomes heralded by the onset of fatigue and exertional dyspnea the ultimate outcome for the patient is in time invariably unfavorable. At this point the treatment of the physician will be directed toward the support of a myocardium which is vainly attempting to maintain an adequate systemic circulation in the face of an unrelenting mechanical stricture. The fort can be held temporarily but eventually under such circumstances both the physician and the myocardium are fighting a losing battle. It is paramount to recognize that the earliest onset of symptoms bespeaks a failing myocardial and pulmonary vascular reserve as the result of *already long-standing structural valvular stenosis*. To repeat, with the onset of symptoms the valvular lesion for the most part has already reached its ultimate cicatrix and progression of the patient's disability is one of symptomatic breakdown and disintegration, not of increasing structural stenosis within the valve itself. The therapeutic conclusion is obvious. The stenotic valve must be opened at the earliest suggestion of the above described obstructive phenomena if one is to avoid the inevitable progression of enlarging cardiac chambers (left atrium, right ventricle, right atrium), pulmonary edema, recurrent hemoptysis, auricular fibrillation, embolic episodes and chronic congestive (right heart) failure.

Clinical Classification

The following classification has been prepared to provide a clinical, functional yardstick paralleling the progressive pathophysiologic changes as outlined above.

Stages of Mitral Stenosis

I. Asymptomatic
II. Statically incapacitating
III. Progressively incapacitating
IV. Terminally incapacitating
V. Irretrievable.

Stage one includes those with the auscultatory findings of mitral stenosis but who as yet have no symptoms. Cases in *stage two* have progressed to the point at which dyspnea and fatigue under physical stress have developed but the patient, with or without medication, living within his own limitations remains on an even plateau. *Stage three*, inevitably the largest group and one encompassing many variables, includes those who, despite the best medical therapy, are slowly losing ground, i.e., are faced with increasing reliance upon diuretics, daily bed rest, etc. In *stage four*, terminally incapacitating, are those patients in whom there is constant evidence of congestive failure even with reasonably limited physical activity. Most of

these can be rendered relatively free of their accumulating tissue fluid only by the strictest of medical regimens, including constant rest in bed. Even then, not infrequently, one is unable completely to reduce hepatic congestion. A certain small percentage of those in this group will ultimately prove after surgery to have been in *stage five* and to have had irreversible pulmonary arteriolar changes. As yet, it has been impossible routinely to separate patients in these two stages by clinical and physiologic methods now available; hence we reserve *stage five* to classify those who, despite a technically adequate commissurotomy, receive no improvement because of irreversible cardiopulmonary pathologic change.

Surgical Objective

It is sufficient to state here that mitral commissurotomy is a procedure in which the individual anatomic leaflets of the stenotic valve are separated. By incising the angles or commissures of the mitral slit, its obstructing effect can be overcome and a considerable degree of valve function can be reestablished. It is to be noted that no valve tissue is removed, thus allowing the liberated though

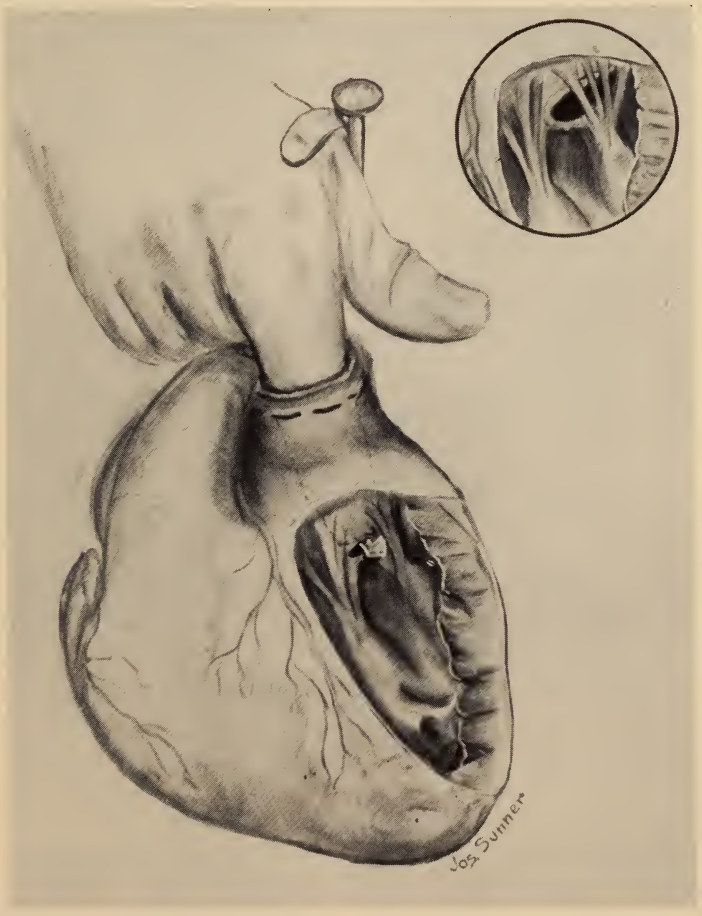

Fig. 1. Sagittal Section through the Left Ventricle to Show the Mitral Valve Cone in Stenosis.

The right index finger and the Glover-Avery guillotine inserted through the left auricular appendage and placed to begin the separation of the anterolateral commissure. The insert depicts the valve orifice after commissurotomy. Note the intact chordae tendineae insuring partial restoration of valve function with prevention of significant insufficiency.

thickened and deformed valve leaflets to open during ventricular diastole and approximate during ventricular systole without the production of additional significant regurgitation (*Fig. 1*).

Indications for Commissurotomy

In the light of the foregoing presentation, the selection of patients for surgical intervention can be simply stated. The *ideal candidate* is the patient with pure mitral stenosis and beginning symptoms of cardiopulmonary dysfunction such as shortness of breath upon exertion. Fatigue out of all proportion to the patient's physical activity is frequently a prodromal or accompanying finding. The mere presence of a well defined mitral diastolic murmur without accompanying symptoms is insufficient reason to suggest surgery, for the operation is not performed primarily because of the murmur but to improve the patient's functional status.

All other indications for commissurotomy are merely compromises from the ideal but for years to come an understanding of the more advanced but altogether salvable states is essential. An outline under seven major categories will most succinctly serve this purpose:

1. History.
   a. Early cardiopulmonary dysfunction—ideal.
   b. Marked dyspnea, hemoptysis, reversible failure—acceptable.
2. Age: Elastic range—physiologic rather than chronological. (Oldest age 61)
3. Valvular defect.
   a. Pure mitral stenosis—ideal.
   b. Associated mitral insufficiency and/or aortic valve lesion in presence of normal left ventricle—acceptable.
4. Roentgen findings.
   a. Left atrium and right ventricle minimally enlarged—ideal.
   b. Minimal left ventricle enlargement—questionable but acceptable.
5. Electrocardiogram.
   a. Normal electrical axis or right ventricular strain—ideal.
   b. Left axis shift—never acceptable.
   c. Auricular fibrillation with controllable ventricular response—acceptable.
6. Functional Capacity.
   a. Stage II (statically incapacitating)—ideal.
   b. Stage III (progressively incapacitating)—acceptable.
   c. Stage IV and V (debatable)—occasional good result.
7. Complicating Factors.
   a. Arterial embolic episodes } Acceptable,
   b. Recurrent hemoptysis } and may be
   c. Pregnancy } urgent.
8. Contraindications.
   a. Acute rheumatic fever.
   b. Subacute bacterial endocarditis until controlled.
   c. Associated marked mitral and aortic insufficiency with all cardiac chambers enlarged.

Analysis of Cases

Five hundred mitral commissurotomies have been performed by the author and his partner, Dr. Thomas J. E. O'Neill. The operative mortality rate for the entire series has been 5.9%. A statistical breakdown of the first 319 of these cases in whom complete data

TABLE 1

MITRAL STENOSIS

STAGES OF STENOSIS	NO. CASES	DEATHS		MORTALITY %	
		Operative	Late	Operative	Late
I. Asymptomatic	0	0	0	0	0
II. Statically Incapacitating	22	0	0	0	0
III. Progressively Incapacitating	213	9	10	4.2	4.6
IV. Terminally Incapacitating	68	7	7	10.3	10.3
V. Irretrievable	16	3	12	20.0	75.0
Total	319	19	29	5.9	9.0

to the present day is available (1 to 5 years) can be seen in *Table 1.* It will be noted that no cases have been attempted in Stage I, and this is as it should be in the present state of such a program. The operation should not be undertaken on the basis of a murmur alone, but for the relief of the patient's functional deterioration of which the murmur is but an auscultatory incident. However, many more than have been in the past should be referred for surgery when in Stage II, for by this time it is obvious that myocardial strain and ultimate breakdown is at hand. Stage III represents an imperative indication beyond which the patient under good care should not be permitted to progress. Stage IV and V, frequently indistinguishable clinically, represent pure salvage on a calculated risk basis and should be subjected to surgery only with the patient's full knowledge and understanding of the risks involved.

The results, as graphically portrayed in *Figure 2*, are self-explanatory. "Excellent" (50%) means that the patient has been restored to a normal, productive life, enjoying normal activities without obvious limitation. A low salt diet and mercurial diuretics are no longer necessary. Most of these have dispensed with the use of digitalis. 30% are classified as improved in that they are objectively and subjectively better as evidenced by their return to almost normal life and activity. Most are under partial medication (digitalis) because of the demands of their more greatly enlarged sphere of activity. A few, terminally incapacitated before surgery, have now become so amenable to therapy that reasonable activity requires digitalization only. The range of improvement in this group varies widely with the condition of the valve found at surgery and the degree to which valve function could be restored. Their progressively downhill course has been abruptly terminated or reversed, some to regain a high level of efficiency and others to remain on an improved plateau.

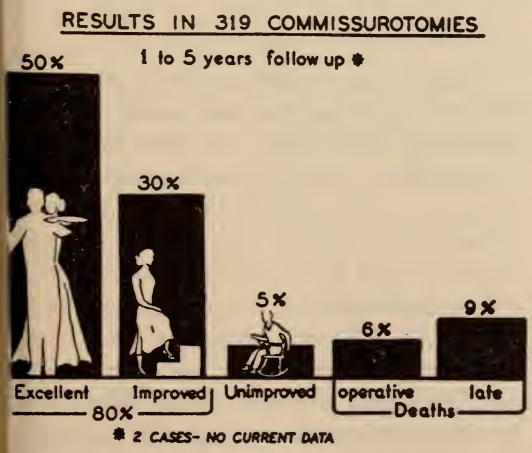

Fig. 2. Results of Mitral Commissurotomy

Seventeen (5%) patients have been essentially unimproved. Multivalvular disease and significant mitral insufficiency, the extent of which was not entirely appreciated until valve exploration, were the major causes for the unsatisfactory outcome.

The operative mortality in the 319 cases closely parallels the mortality in the entire series and was 5.9%. As might be expected, the deaths occurred in the more advanced stages of the disease (*Table 1*), and were due primarily to the unyielding nature of the valvular pathology or to improper technique as applied to the pathologic state present (operative, anesthetic and diagnostic). The late deaths were all occasioned by the presence of pre- and post-operative irreversible cardiovalvular and pulmonary-hepatic vascular (and parenchymal) disease which remained unaffected by the mere relief of mechanical obstruction and progressed to their normal termination.

Aortic Stenosis

The problems associated with the surgical alleviation of aortic stenosis have to date presented far greater difficulties than any of the other stenotic valvular lesions. There are a number of reasons for this.

Anatomically, the valve is the least accessible to exploration, for it lies centrally placed within the confines of the heart. In

aortic stenosis, the left ventricular myocardium is greatly hypertrophied, which, together with the tremendous vascular pressure generated within its outflow tract, prevent the use of a subaortic transmyocardial incision for the insertion of finger or instrument similar to that used in pulmonary valvulotomy, because of the ensuing uncontrollable hemorrhage. The valve cannot be effectively reached through an auricular appendage. The position of the ostia of the coronary vessels lying directly behind the valve leaflets makes direct reconstructive surgery hazardous.

Pathologically, there is an early fusion of the three valve cusps, the margins of which become thickened, rolled, eburnated and infiltrated with calcium very early in the course of the disease. This is due, in part, to the disease itself but more particularly to the location of this valve in the course of the blood stream. The valve lies in a confined space of small diameter and is the recipient of the full head of vascular pressure from the strongest of contracting cardiac chambers—the left ventricle. The factor of vascular *trauma* is, therefore, of great importance for, following initial fibrotic agglutination of the cusp margins, there is a constant and steady deposition of traumatic elements such as fibrin and calcium from which there can be no relief. Thus, calcification develops early and as the leaflets are relatively small in surface area, almost complete immobility and fixation may be rapidly evident. Some flexibility of the cusps at their attachment to the aortic ring may remain for a time but this is less prominent than that seen in the stenotic mitral valve. This factor of *trauma* no doubt partially explains the fact that the antero-medial leaflet of the mitral valve (also called the aortic or septal leaflet) is the seat of the greatest calcification in mitral stenosis, for it lies nearest the aortic ring in the high pressure left ventricular outflow tract and also receives the brunt of the vascular ejection at the time of left ventricular contraction. Therefore, from a pathologic standpoint, surgical intervention in aortic stenosis, to effectively restore a measure of normal valve leaflet motion, must be carried out before extremes of the above described process are reached. To wait longer merely compounds the likelihood of surgical failure, for in consequence of the valvular change the left ventricular myocardium hypertrophies and dilates, in due time to wear out and become incapable of effective action. As the left ventricle is the cornerstone of the heart and circulation its failure predicates irremedial disaster. This is in contrast to the findings in mitral stenosis, where, despite profound pathological and clinical changes even to the point of prolonged congestive failure and invalidism, the left ventricle retains its indispensable function—actual, compensatory and recuperative—almost to the end.

Physiologically, because of the jet-like ejection of relatively small amounts of blood with each left ventricular contraction, the systolic blood pressure may not reach high levels although it is perhaps sustained and maintained longer than usual. Diastolic pressures, however, are high so that the pulse pressure is small and coronary artery filling, now under greater stress because of the demands of an increased myocardial mass, may be inadequate. As such, these patients are often precarious anesthetic risks, to say nothing of the superimposed danger of surgery.

Surgical Objective

Despite these apparent roadblocks, considerable progress has been made. The experimental work which has been undertaken in an effort to find a satisfactory surgical solution to this problem has been previously reported (11). Briefly, the present operative approach calls for a left lateral thoracotomy, the introduction of a dilating instrument through a relatively avascular area of the left ventricle near its apex and lateral to the left descending coronary artery. The dilator is directed through the valve by passing it over a previously placed wire guide, the olivary tip of which can be felt in the aorta

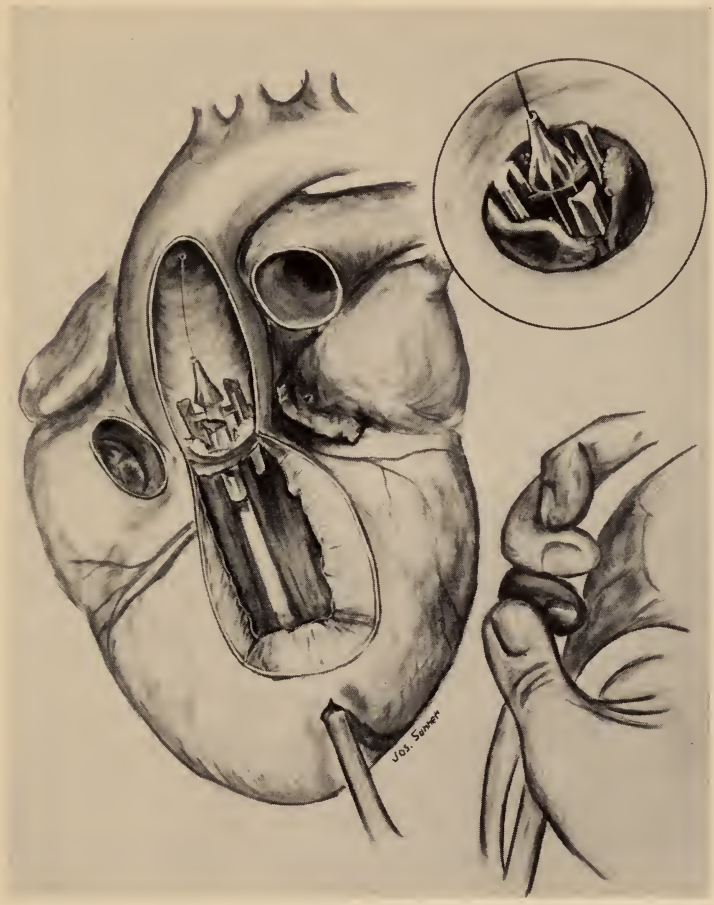

Fig. 3. The Aortic Dilator Inserted through the Myocardium of the Left Ventricle Near Its Apex. This instrument is guided through the aortic valve by threading it over a fine olive-tipped wire previously placed through the valve. The insert depicts the three flanges of the dilating head separating the commissures. The self-rotating head settles automatically into the V-shaped commissures of the fused aortic cusps.

prior to the insertion of the larger instrument through the myocardium. The dilating head opens in triangular fashion causing the fused commissures of the stenotic valve to separate, partially relieving the stenotic obstruction and restoring a measure of valve action (*Fig. 3*).

Clinical Classification

The necessity for translating the present rationale of surgery for aortic stenosis into reasonable, practical language has called for the development of a classification for the recognition of clinical states either applicable or unsuitable for surgery at the present time.

The recognizable clinical stages through which the average patient with aortic stenosis will pass are well known, although perhaps not readily defined in the mind of the physician in the light of surgical advances. *Stage I* is the period during which the typical systolic murmur develops before symptoms result. *Stage II* marks the onset of an ill-defined period where the patient becomes subjectively aware of his forceful heart action, palpitations develop, easy fatigue becomes noticeable and his attention may be called to the unusual, visible pulsations in his supraclavicular and suprasternal notches. Admittedly, this stage is not specifically characteristic of aortic stenosis *per se*, but when seen with an aortic systolic murmur the combination takes on

added significance. *Stage III* ushers in the obvious period of progressive disability due to a diminishingly effective cardiac output as evidenced cerebrally by spells of dizziness and actual syncope. Myocardially, substernal discomfort, tightness, effort angina with its characteristic distribution bespeaks of inadequate coronary flow. With beginning left ventricular failure, *Stage IV* is characterized by episodes of pulmonary congestion and edema at first rather easily controlled by medical measures but shortly to become refractory to even the most vigorous management. *Stage V* connotes impending disaster and an early demise for right heart failure with hepatomegaly, ascites and peripheral edema labels the heart picture as one of irretrievable damage not to be reversed by any regime—medical or surgical.

Results of Surgery (Table 2)

Twenty-two cases have undergone aortic commissurotomy and six of these have been combined with a mitral commissurotomy because of concurrent bivalvular stenosis. One patient (Stage II) done over three years ago remained completely asymptomatic for two years. During the past 12 months, although working steadily and living a normal life, he has noticed some minor precordial tightness with exercise after meals which had not been present during his first two postoperative years. This patient's aortic commissurotomy was performed with our original dilator (2) which did not have the strength or wide diameter opening of the present more refined instrument which may account for his present status. Clinically there has been no change in his cardiac findings.

The remaining twenty-one cases have been operated upon in the past eighteen months. The pertinent data can be seen at a glance in *Table 2*. The overall mortality has been high, which may have been influenced somewhat by the inclusion of cases with bivalvular surgery. The observation of paramount importance, however, is that cases done in the early symptomatic phases (12 cases—Stages II & III) run a risk of only 8.3% and even including those in Stage IV, when pulmonary edema has entered the picture the mortality rate is a reasonable 11.7%. One has only to consider the seriousness of the disease and the utter hopelessness of its immediate prognosis to appreciate that such results are highly encouraging at this stage of our surgical programme. When true congestive failure has developed (Stage V) it is doubtful whether much, if any, salvage can be either expected or obtained.

Conclusions

The natural course and progression of rheumatic stenotic valvular disease has dictated the necessity for the mechanical relief of its acquired stricture. Mitral and aortic commissurotomy have become major adjuncts in the overall and continuing care of victims so afflicted. Provided the patient is referred for surgical intervention early in the course of his symptomatic progression, such a patient can be restored to a high level of efficiency and enjoy a more normal life as a useful and productive citizen. The burden of selecting pa-

TABLE 2
Aortic Stenosis

	NO.	EXCELLENT	IMPROVED	UNIMPROVED	DEATHS
I. Asymptomatic—murmur only	0	—	—	—	—
II. Fatigue, Heart Consciousness, Palpitations	2	2	—	—	—
III. Syncope, Angina	10	2	6 (3*)	1	1
IV. Episodic Pulmonary Congestion	5	—	3	1	1 (1*)
V. Congestive Failure	5	—	—	—	5 (2*)
Total	22	4	9	2	7

tients at *an early stage* rests squarely on the shoulders of the practicing physician and this responsibility can no longer be avoided or postponed.

REFERENCES

1. Bailey, C. P., Glover, R. P., and O'Neill, T. J. E.: Surgery of mitral stenosis, J. Thoracic Surg. **19:** 16, 1950.
2. Glover, R. P., Bailey, C. P., and O'Neill, T. J. E.: Surgery of stenotic valvular disease of the heart, J. A. M. A. **144:** 1049, 1950.
3. Glover, R. P., O'Neill, T. J. E., and Bailey, C. P.: Commissurotomy for mitral stenosis, Circulation **1:** 329, 1950.
4. Glover, R. P., Bailey, C. P., O'Neill, T. J. E., Downing, D. F., and Wells, C. R. E.: The direct intracardiac relief of pulmonary stenosis in tetralogy of Fallot, J. Thoracic Surg. **23:** 14, 1952.
5. Glover, R. P.: Stenotic valvular disease of the heart: surgical treatment. Texas State J. Med. **48:** 674, 1952.
6. O'Neill, T. J. E., Glover, R. P., and Bailey, C. P.: Commissurotomy for mitral stenosis, J. Internat. Coll. Surgeons **13:** 355, 1950.
7. O'Neill, T. J. E., Glover, R. P., and Bailey, C. P.: Observations on the surgical treatment of mitral stenosis by commissurotomy, J. A. M. A. **147:** 1032, 1951.
8. Glover, R. P., O'Neill, T. J. E., and Bailey, C. P.: Mitral stenosis; its surgical treatment by commissurotomy, Pennsylvania M. J. **53:** 375, 1950.
9. Janton, O. H., Glover, R. P., O'Neill, T. J. E., Gregory, J. E., and Froio, G. F.: Results of the surgical treatment of mitral stenosis: analysis of 100 consecutive cases, Circulation **6:** 321, 1952.
10. Glover, R. P., O'Neill, T. J. E., Harris, J. S. C., and Janton, O. H.: The indications for and the results of commissurotomy for mitral stenosis, J. Thoracic Surg. **25:** 55, 1953.
11. Bailey, C. P., Glover, R. P., O'Neill, T. J. E., and Redondo-Ramirez, H. P.: Experiences with the experimental surgical relief of aortic stenosis: a preliminary report, J. Thoracic Surg. **20:** 516, 1950.

Isotope Dilution: a Theory, a Method, a Pathway to New Horizons*

By FRANCIS D. MOORE†, M.D.

DURING the past ten years the development of isotope dilution techniques has permitted us to view an opening vista through the many varieties of body composition found in normal man, and the patterns of disorder produced by disease. It is our purpose tonight to trace briefly the history of the origin of these methods, mention their present status, and discuss briefly their future potentialities.

As a first step, it is necessary to spend a moment on the concept of body composition. The human body obviously contains finite weights of certain substances. There is a certain amount of water in the human body which can be expressed in cubic centimeters, milliliters or liters. Varying inversely to the amount of water is a finite amount of fat, by which we mean depot neutral fat such as is found subcutaneously and in the omental and mesenteric fat depots. Then there is the skeleton. This great system of insoluble salts is quite heavy and its weight can of course be expressed in grams or pounds. Moving the skeleton about, and therefore moving us about, is a finite mass of lean red tissue, largely striated muscle. This is the energy-exchanging protoplasm of the body whose support, under conditions of heavy work, may require 3000–4000 calories per day. The weight of certain visceral organs has been known and measured for years; every pathologist in his time-honored protocol for postmortem examination measures the weight of the liver, the kidneys, the spleen. But the weight of water, fat, skeleton, muscle, which may all have been profoundly affected by the disease process, is not measured. There is a certain amount of electrolyte in solution in body fluid (an amount expressed in units of weight) whose dislocations profoundly disturb our health. We could enumerate such examples indefinitely, including such things as the total weight of skin, the total weight of trace metals, the total weight of carbohydrates or small-molecular-weight-nitrogen-containing compounds.

Such enumeration would be fruitless for our present purpose which is to focus our attention on the body as containing within it measurable weights of certain substances and families of substances which, taken together, constitute body composition.

In recent years we have thought largely in terms of peripheral concentrations, such as the serum sodium or protein concentration; or the peripheral concentration of red blood cells measured by hematocrit, hemoglobin concentration or red blood cell count. Such measurements are of course of great importance; the concept of body composition merely looks one step further and asks "how much sodium is in the body?", "what is the total mass of red blood cells, and the total volume of plasma in which they are suspended?"

This concept of body composition and of compositional changes produced by disease is obvious enough and is of course not new. It was apparent to early workers such as Vesalius and Sanctorius who wondered, the one from an anatomical and the other from a physiologic point of view, how much "stuff" there was in the human body and what this material was. It has been the advent of dilution methods in general and isotope dilution principles in particular which have permitted us for the first time to measure some of these

* Alvarenga Prize Lecture XIII (Award XLVIII), College of Physicians of Philadelphia, 4 November 1953.

† Surgeon-in-Chief, Peter Bent Brigham Hospital; Moseley Professor of Surgery, Harvard Medical School, Boston, Mass.

gross weights in the living patient. Prior to the advent of these methods, some work had been carried out on cadavers in which, by desiccation methods, total water was determined; total fat had been determined on small samples of tissue as had also total electrolyte. None of these was a method applicable to the living patient.

The Dilution Principle

If a known weight of solute is placed in an unknown volume of solvent and the concentration of solute determined after adequate mixing and stirring, the unknown volume has thereby been measured. For instance, if one has a beaker containing water of unknown volume and places within it 1.0 gm. of sodium chloride, he may then stir it up to provide complete mixing. If, after mixing, the concentration is .01 gm. per cc. it is then clear that the amount of fluid in the beaker is 100 cc. This is the dilution principle and it is expressed by the formula

$$C_1 V_1 = C_2 V_2$$

$$\therefore \quad V_2 = \frac{C_1 V_1}{C_2}$$

where: C_1 is the concentration before mixing, C_2 the concentration after mixing; V_1 the volume before mixing and V_2 the volume after mixing.

The product of concentration and volume has the dimension of mass or weight and therefore this formula merely tells us that the mass of the solution being dissolved is the same before and after mixing in a large volume. The term "tracer" can be used for the substance mixed up and dissolved. It is a good word since it can apply to a color tracer such as the Evans Blue dye, a tracer known by weight such as deuterium, or a tracer detected by radioactivity measurements such as radiosodium.

Early Applications

Indeed, it was the use of the dye to measure plasma volume which marked the first application of this dilution principle to human body compositional study. In 1915 this principle was first used by Keith, Rowntree and Geraghty for the measurement of the volume of plasma using a red dye which was thought to dilute itself largely in the plasma volume. This method evolved over the years and the red dye became replaced with the blue dye chemically indicated as T-1824, otherwise known as Evans Blue because of its initial study by Professor Herbert M. Evans of California. This dye was easier to read on the colorimeter and appeared to measure the volume of plasma. More recent evidence has indicated that this blue dye actually "dyes" the plasma protein, making a bond preferentially with plasma albumin, and it is in a sense a tracer for albumin. It measures the "albumin space". When the time of dilution is taken quite early in the disappearance curve (under an hour), the dye is largely confined to the plasma volume and its dilution measures that volume. Little further developed along these lines until in 1934 the thiocyanate method for measuring the extracellular volume was developed by Crandall and Anderson. Here the assumption was that the thiocyanate ion, acting in a sense as a tracer for chloride, diluted itself in a mass of body water largely extracellular in position. The method had great value and although it has been superseded by a variety of other methods, the principle remains an important one.

This is about where matters rested until in the early 1940's radioactive and stable isotopes became available. It is with these substances that we have been able to measure the total body water, the total exchangeable sodium and the total exchangeable potassium, the three methods to which we are going to devote most of our attention tonight. Before turning to them, however, it is important to re-emphasize certain fundamental principles of the application of tracer dilution methods in biology.

The Dilution Principle in Biological Work

If a tracer is to be used for a dilution technique in such a complex system as the mammalian body, whether for the measurement of a volume or of a mass, the first principle which must be obeyed is that "*the tracer must behave as the traced*". If one is using a tracer to measure the body sodium, the tracer involved must behave exactly as sodium does. This of course is quite an easy requisite to satisfy in dealing with such a measurement as total exchangeable sodium when measured with radioactive sodium. Since it is one of the premises of all isotope research that the addition of one unit of atomic weight does not change the chemical characteristics, providing atomic number is unchanged, we assume that biological systems cannot differentiate between sodium 23 and sodium 24 except by virtue of radiation. This obvious principle, however, is less easy to satisfy in certain other of these methods. For instance, in an extracellular method such as the thiocyanate method for extracellular volume, it is disconcerting to find that in certain cells of the body, such as for instance the gastric parietal cell, the thiocyanate does not remain extracellular. And in some of the early methods for total body water based on the dilution of such substances as urea or sulfonilamide, one was dealing with an organic molecule which was metabolized and excreted in a selective way entirely different from the body's handling of water.

The second principle might be stated as follows: "*The tracer must dilute itself in a stable volume or mass*". Thinking back to our original analogy of some salt in a beakerful of water, this principle tells us that the beaker must have no very significant leak. If we try to carry out a dilution method in a hose through which water is running at a rapid rate, we will not discover the volume of the hose very effectively. We must be dealing with a stable volume. In the case of the plasma volume method and the extracellular volume method, this second principle is often violated. This principle is violated because the water and solutes in the plasma are constantly exchanging with the extracellular fluid, and certain of the ions in extracellular fluid are in a constant state of flux with the cell. For this reason, there is a current running through the volume to be measured and the actual magnitude of the current may be large enough to distort the volume measurement. In certain other of the methods we are going to discuss, this principle is very closely adhered to. Of all the methods for tracer dilution, the methods now available for the measurement of the red cell mass are among the most perfect. The red cell volume is indeed a stable volume (viewed in terms of changes over a period of days) and its measurement most satisfactorily answers this requirement.

The third principle to be satisfied is that "*the concentration of the tracer must be easily measurable at equilibrium*". This principle has two ideas implicit in it: first, that the concentration of the tracer must be *measurable*, and second that an *equilibrium* of mixing or distribution must be attained. It is the first idea here which is of course responsible for the extensive use of isotopes in this field. If one adds a pinch of ordinary chloride to the body's chloride pool it is immediately lost and there is no way of identifying this added chloride nor of discovering the mass of chloride in which it has been diluted. But if a tracer such as isotopic chloride is used, its measurement is a matter of comparatively little difficulty, thanks to the physicists. The *equilibrium* concept is a very basic one and simply states that after a period of mixing, the time-concentration curve of the tracer must be reasonably "flat". In other words, there must be a matter of minutes or hours or even days in which, dilution and mixing having occurred, the concentration does not markedly change. This principle is extensively violated in certain of the plasma volume methods where there is never a flat plateau of dilution-equilibrium. It is particularly violated with some of the extracellular methods such as inulin or thiosulfate, wherein

glomerular filtration so rapidly removes the tracer from the pool to be measured that very elaborate methods of constant infusion or of mathematical extrapolation must be used. In the total body water and total electrolyte methods to be discussed tonight, this principle is very nicely fulfilled and again referring to the red cell mass methods, it is most perfectly fulfilled.

After one of these methods has been developed, there are two other principles which should be satisfied. First, that a *chemical check* on the accuracy of the method should be obtained, and second that it should be *reproducible and accurate.*

As to the first of these, the *chemical check*, little further need be said save that one should have a way of proving that the mass or volume measured is in truth what one thinks it is. We will encounter this chemical check later in our discussion and will not go into it further save to point out that in the case of the extracellular volume method, this chemical check is literally impossible. There is no way of taking a cadaver or even a mass of tissue and determining directly how much of the fluid in it is outside of cells. As to *reproducibility, reliability and accuracy*, these are of course matters which pertain to any chemical method. But they are all too often lost sight of in the tracer dilution techniques. Once a method of this type is established, one should be able to take a normal individual and measure the same entity on him every week for many months in a row and come out with essentially the same answer. If this criterion cannot be obtained, it is idle to attempt to apply the method to sick patients. The violation of this principle has been responsible for much reported work of little value.

Total Body Water

After working in clinical research for several years with methods for the measurement of the plasma volume, the red cell mass and the extracellular phase, we undertook to try a tracer method for total body water. Water, hydrogen hydroxide, is a simple molecule consisting of only two elements. Clearly, the most suitable method for measuring its volume would be a tracer for one of these elements. Attempts to measure body water by the dilution of organic complexes had a brief flurry in the 1930's and indeed has been revived again in recent years. But from a theoretical and practical point of view, its most accurate measure would certainly come from an isotope of either hydrogen or oxygen.

In 1944 it occurred to us to try to secure some heavy water (deuterium oxide, D_2O) for early experiments in this field. We did not realize at the time that heavy water was being made in huge quantities as one of the necessary prerequisites for certain types of atomic weapons development. Nor did we realize that at about that time the R.A.F. was planning to bomb and destroy a great heavy water plant used by the Nazis in Norway. Suffice it to say that we were able to obtain a small amount of heavy water and start our initial exploration.

Heavy water, D_2O, is a water formed by the combination of deuterium with oxygen. Other tracers which might have been used are isotopes of oxygen, or the radioactive isotope of hydrogen of mass 3, tritium. The oxygen isotopes were not available to us at the time and their half-lives are unfavorable. Tritium was likewise not available although it has since been explored for this purpose.

We initially injected some heavy water into the blood of rabbits and let it come to dilution equilibrium. We then measured its concentration on a very simple physical apparatus known as a gradient tube. Not being physicists, we were very clumsy with this physical measurement of deuterium concentration. Deuterium is not radioactive, it is only heavy. And its excess weight is truly tiny. At the concentrations which we were using, it increased the specific gravity of water only by several units in the 7th decimal place. However, in using a small animal such as the rabbit we were unknowingly very fortunate, for with the small amounts of deuterium we had available, we could inject enough into

the rabbit to produce quite a high blood deuterium concentration so that our crude method of measurement could give us a reasonably accurate answer. Later, in working with a 70 kilogram man (instead of a 1 kilogram rabbit) where we could not obtain such high deuterium values, we soon found that much more accurate instrumentation was required.

Having measured the deuterium concentration in the rabbits' blood after several hours, we then sacrificed the rabbits and heated them to dryness in a hot oven. By the change in weight, we determined directly the amount of water in the body, and it was with great gratification that we found that deuterium indicated about the same weight of water in the animal's body as the drying technique had. We then went ahead with early studies in the human being. This was in 1945 and a preliminary report of this work was published in 1946. But our stumbling and halting steps in instrumentation are best summarized by saying that it was not until 1949 that we were able to obtain a series of reproducible and satisfactory results. The instrumentation involved is quite beyond the scope of our talk tonight. Suffice it to say that there are at least half-a-dozen ways of measuring deuterium concentration and that we finally have picked one of the simpler, namely the falling drop. Through the kindness and cooperation of the biophysical laboratories at Harvard Medical School under Dr. Arthur K. Solomon, we have been able to check this against the most accurate method—although the most complex—namely the mass spectrometer. We find that the falling drop method, while complex and tricky, is just as accurate and indeed more rapid than the other.

There is nothing new under the sun and that was true also of deuterium research. After several years of working in the field, we became aware that in 1934, shortly after heavy water was first isolated and described, two British scientists, Hevesy and Hofer, published a short communication in the British scientific journal, *Nature*. In this they described how, one day while they were drinking tea, they speculated on how interesting it could be if some of the tea were made with heavy water. They realized then that such an experiment might tell them about how long a molecule of water remained in the human body and indeed might tell them how much water was in the human body altogether. One or two experiments were done in small animals but with the scarcity of the material at the time, nothing further was done and indeed the concept itself lay buried in the literature, known only to a few British physicists who were unconcerned with immediate biological application.

Turning now to our "principles", it will be of interest to see how the heavy water method satisfies them. First, does the tracer behave as the traced? The answer to the purist is "No." Deuterium has twice the mass of hydrogen and it has been shown again and again to behave differently than hydrogen. It is less diffusible, less volatile. When the hydrogen of the body is about 30% replaced with deuterium, an animal shows marked toxic symptoms which are of themselves of great interest: exophthalmos, excitement and death in convulsions. Surely, this is not a perfect tracer! On the other hand, at the extremely low deuterium concentrations used (about 0.15 atoms per cent greater than ordinary D), it is very difficult indeed to detect any difference in metabolism of deuterium and hydrogen. There is no evidence available at present that so-called isotope effects or biological differences due to nuclear mass have played any particular role in distorting the measurements.

Turning to the next principle, does the deuterium dilute itself in the stable volume? As far as body water is concerned, the answer is a most enthusiastic "yes". Body water is a very large volume, about 50 quarts in a normal sized man, and its exchange with the environment while physiologically important

is actually quite small: only about 4% of total body water exchanges with the environment per day. So the volume is quite stable. But in the case of the hydrogen ion and the hydroxyl ion, there is one other loophole. The hydrogen and hydroxyl ions of many organic compounds readily exchange with the hydrogen and hydroxyl ions of water. And indeed the hydrogen of water may exchange with other radicles such as NH_2 or COOH. So the question arises as to whether or not deuterium dilution measures a much bigger mass than body water, namely body water plus non-aqueous exchangeable hydrogen. The evidence suggests that while the deuterium method definitely does measure "total exchangeable hydrogen", the non-aqueous exchangeable hydrogen is a tiny fraction of the whole. While of great importance and interest to the physical chemist and the organic chemist, it is in point of total mass so small as to affect very little the measurement of the total body water.

Is the deuterium concentration measurable at equilibrium? Of all the methods we will discuss tonight, deuterium dilution is possibly the most satisfactory in this regard. There is no reason either *a priori* or on the basis of laboratory evidence to expect that the water of the blood plasma or the urine is other than in equilibrium with the rest of body water. So that after the material is mixed, which takes about an hour*, blood samples are taken and the blood deuterium determined.

We have already mentioned the physiologic check based on the drying out of rabbits. And as to reproducibility and reliability, we have here a method which in our laboratories has now been applied in almost 1000 instances. The reproducibility of values in the normal subject is most gratifying.

Our next step was to explore this method in both sexes throughout the life span. There is not space here to discuss all these ramifications in detail yet the two years spent in the study of the normal were amongst the most profitable ever spent in our laboratory and three very interesting findings emerged from our study of the normal. The studies of very sick patients which followed have only had meaning in relation to predicted values for the normal. First, we found that little babies are very watery. Just where this water is, we do not know. Many young infants appear to be very fat, or at least pudgy. But from our data, it would appear that they are not so much fat as they are well watered down. We have not pursued this matter farther but the high total body water of small infants remains an interesting and, in a sense, an unexplained finding. Secondly, we found that in old age the total body water tends to drop off. For many years, the thought of older people as "dried up" or "wizened" has of course been a part of our literature. The fall in total body water in the older age group, however, is not spectacular and may in part be due to an excess accumulation of fat, especially in the older female. Our third finding, in our study of the normal, was that at puberty the male and the female assume a very different body composition. Up to that time total body water has been the same in the two sexes, but at puberty, with the advent of other secondary sex characteristics, the female grows bigger but does not accumulate very much more water, whereas the male grows bigger and does accumulate much more water. This appears to be due to the fact that the accumulation of fat, particularly subcutaneous fat in certain parts of the body, is a sex character of the female and it is axiomatic in this work that body storage neutral fat contains very little water. The only water it contains at all is the extracellular water around the fat cells. Whereas the male as a secondary sex character develops a great deal of striated muscle. This muscle is 73% water and seems to account for this

* In certain pathologic states, such as edema or ascites, the equilibrium may require 3 to 6 hours for its attainment. Serial blood samples are then obtained to establish that equilibrium has occurred.

sex difference. An example of "steroidal growth".

Total Body Electrolyte

Thus far we have been discussing the dilution of a substance in a fluid such as a dye in plasma volume, thiocyanate in extracellular water or deuterium in body water. In discussing deuterium dilution in body water we have pointed out that we are really measuring the total exchangeable hydrogen.

Turning to other body electrolyte, we find a concept which is an extension of our familiar dilution principles. We dilute an isotopic solid in a mass of similar solid and determine by dilution the weight of solid in which the isotope has been diluted.

In introducing the other methods, we mentioned a beaker full of water. Here we might change our analogy and imagine a pail full of bird shot. The bird shot is gray. Now, if we add to that pail a known number of bird shot painted red, and mix these bird shot evenly throughout the pail, we can then take out a fair sample and by the number of gray shot found with each red shot, we can calculate the total number of gray shot in the pail by our same dilution formula. This extension of the dilution principle is basic to the measurement of total body electrolyte. For instance, in the case of potassium, we inject radioactive potassium and let it equilibrate throughout the body potassium and then measure its concentration in ordinary potassium. The same for sodium.

We will discuss the two methods separately.

Total Exchangeable Potassium

Our initial exploration of this method consisted in injecting radioactive potassium (K^{42}) into the body, letting it equilibrate for about 24 hours and then measuring the concentration of radioactive potassium in normal potassium in the red blood cells. The concentration of radioactive isotope per unit weight total element is referred to as "the specific activity" of the radioactive substance. For instance, if one has one microcurie of K^{42} for each milligram of K^{39} *, we may refer to the specific activity of this potassium as being 1 microcurie per milligram and this specific activity ratio is a representation of the *concentration of radioactive isotope per unit naturally-occurring isotope.*

The physical concept was quite sound but our first biological step was in error for we soon found that the red cell potassium is a very special division of body potassium and does not reach equilibrium with other potassium in the body until many hours or even days after injection. So that set us off on a hunt to find out where in the body we could measure potassium and satisfy our third principle, namely of having a tracer measurable at equilibrium. We studied radiopotassium equilibrium in muscle, in blood, in urine, in plasma, in skin and in other tissues. These studies were all carried out in patients who were injected with the isotope shortly before surgical operation, at which time tiny samples of tissue were taken for analysis. We found that all the body tissues we studied were in equilibrium of exchange with potassium by 24 hours, with the exception of the red blood cell. Indeed, equilibrium is obtained much sooner than that in many tissues but at 24 hours a general equilibrium has been attained. And we found that the potassium either of urine or of blood plasma was quite satisfactory for the measure of the equilibrium specific activity.

As to our other principles, there was no question that the tracer behaved as the traced. And the total mass of body potassium is quite large—about 3000 meq. or 120 gm. and the total flux with the environment is only 100 meq. a day or about 3 per cent. The total mass is therefore stable.

To check this measurement, we measured the total body potassium of small animals, after measuring their radioactive potassium dilution mass, and found good corroboration.

* We use the symbol K^{39} to signify the mixture of normally-occurring potassium isotopes in the body.

The radioactive method does not measure all the body potassium in 24 hours because of the small amount of potassium in red cells which has not exchanged, and there is a possibility that some of the potassium in bone may not have completely exchanged at that time. But our evidence suggests that the K^{42} dilution method, using a 24 hour equilibration point, measures approximately 98% of body potassium. We might call the method "total body potassium" but it seems more conservative and accurate to call it "total exchangeable potassium" since that is truly what we are measuring. The normal value here is approximately 47 meq. per kg. of body weight in a normal adult male. We have not yet studied the normal value in children because there is some hesitancy to use radioactive isotope tracer methods in children. The present development of better technology for counting radioactive materials may make this much-needed normal study more readily attainable.

Recalling the sex differential in total body water, we studied it here and found that the normal female has a good deal less potassium than the normal male. The normal value for the adult female is about 41 meq. per kg. This checks out very nicely with the total body water method and is probably to be explained on the same basis, namely that as the female reaches puberty, further body development is not devoted to making big muscles, whereas in the male it is. It is the red striated muscle tissue of the body which contains the great fraction of potassium and of oxidizing protoplasmic mass. We have come to feel that the measurement of the total exchangeable potassium (symbolized by the letters K_e) is truly a measurement of a mass which is proportional to the "lean body mass". It is proportional to the mass of tissue actively engaged in energy exchange.

The distribution of potassium in the body is very lop-sided. Of the 3000 meq. potassium present in the normal male, only about 65 meq. or 2% is in the extracellular phase, and less than 1% is found in the plasma itself. All the rest resides at high concentration in body cells. Indeed, it is one of our principle findings, in studying sick patients, studies which we will not detail here, that the changes in plasma potassium concentration often do not parallel and do not reflect changes in total potassium.

Total Exchangeable Sodium

Turning now to the measurement of total exchangeable sodium, we find a number of interesting and contrasting problems. We did not commence the investigation of this measurement until several years after the potassium measurement had been perfected and normals defined. Because of the fact that most of the soluble sodium in the body is in the extracellular phase, it would seem no problem to inject radiosodium and let it reach equilibrium, then measure the equilibrium familiar formula. However, as we began to apply our basic principles to this method, we found a number of problems arising.

As to principle No. 1, since we are using radioactive sodium, we are dealing with an excellent tracer for normal sodium and there is no question about validity on this score. The same is true of our second principle, namely that the tracer must dilute itself in a stable volume. It has been known for some time that there is approximately 2500 to 3000 meq. of sodium in a normal man. The flux with the environment is only about 100 meq. per day so that we are dealing with a stable volume.

When we turn to the matter of equilibrium, we encounter a new problem. When radiosodium is injected into the blood, it seems to achieve a sort of equilibrium very rapidly. Even as early as 20 minutes after injection, the time-concentration slope is not very steep. But it continues to fall gradually for many hours. Indeed, this gradual fall can only be interpreted as meaning that the sodium is equilibrating into a mass of body sodium that is probably not too intimately related to the plasma. Since the total exchangeable sodium

is inversely proportional to the equilibrium specific activity, this gradually falling sodium concentration indicates a gradually rising figure for total exchangeable sodium.

When we follow the curve out to about 24 hours, we find that an equilibrium has been attained. After this time there is relatively little further change. Now the question arises, into what areas has the radioactive sodium penetrated?

It was the solution of this question which took us considerable time. It has been known for many years that a great deal of our body sodium is in the skeleton. It is in bone and it is in insoluble salt of bone which cannot be leeched out merely by placing the bone in water. These sparingly soluble sodium salts are very interesting inorganic compounds and they seem to be related to the crystal lattice structure of bone cortex. To study this problem, Dr. Edelman of our laboratories took small samples of bone from animals which had been injected with radioactive sodium many hours before. In addition, we were able to take samples of bone from patients having thoracic operations, in which rib was removed. This bone was then analyzed for total sodium and for radiosodium. We soon discovered that somewhat less than half of the sodium in the bone has exchanged with the radioactive isotope at 24 hours. Ordinary radioactive sodium (Na^{24}) has a half-life of only about 15 hours. This means that after injecting it into an animal in reasonable dosage, it is rather difficult to measure the concentration of the material on radioactivity detecting equipment much longer than 36 hours after it is injected. We wished now to see if the radioactive sodium equilibrium curve was possibly different from any other curve we had observed, with a slope going on for many days or even weeks until finally all the bone sodium was exchanged. For this reason, some long-lived sodium (Na^{22}) was obtained, injected into animals and the time concentration curve both in blood and in bone was followed out for three weeks. We found that there was little change after 24 hours and that about 45% of bone sodium was exchangeable ultimately.

It is very important to realize that this is only a partial conclusion. The sodium which is in our bone as adults all came from the environment. We cannot create sodium ourselves! And therefore every bit of it must at one time have been "exchangeable" with dietary sodium. We hypothecate that after this sodium gets into the bone in a certain insoluble salt, it ceases to be readily exchangeable with the environment; possibly only diseased states, actual bone disruption or further bone growth release any of this sodium. It is difficult to conceive of a substance in the body which is non-exchangeable over a period of many months or years. Whether this is true of the bone sodium cannot be stated with certainty now. All we can state is that up to three weeks, only 45% of bone sodium is exchanged and no further alteration in the curve is demonstrable. Indeed, that is all we need to know for the total exchangeable sodium method. We can state that the total exchangeable sodium, when based on equilibrium specific activity in the plasma at 24 hours, measures a weight of sodium in the body which includes all the extracellular sodium, what little sodium there is in soft tissue cells, and somewhat less than half the bone sodium.

This is the "available" sodium. Possibly it is the "soluble sodium". This is the important sodium from the point of view of meeting the life-endangering emergencies of injury, surgery and acute disease. The total exchangeable sodium in man is about 41 meq. per kg. and in females is only slightly smaller, averaging between 39 and 40 meq. per kg. In our other indices of body composition, we have found that the female had less total body water and less total body potassium. In the case of sodium, however, the measurements are about the same.

Normal Values and Their Significance

Using these indices of body composition we find normal values as follows:

	MALES	FEMALES	UNIT OF EXPRESSION
Total Body Water	62 (54–70)	52 (44–60)	Per cent of Body Weight
Total Exchangeable Potassium	47 (25–54)	40 (28–48)	Meq. per kilogram
Total Exchangeable Sodium	41 (36–46)	40 (24–46)	Meq. per kilogram

All figures are for young adults. Figures in parentheses indicate the range of values.

We have not discussed in this paper the development of the methods for plasma volume, red cell volume and extracellular water. All of them are dilution methods of great interest and importance. The normal values for these measurements are as follows:

	MALES	FEMALES	UNIT OF EXPRESSION
Plasma Volume (Blue Dye)	4.0–5.0	3.5–4.5	Per cent of Body Weight
Red Cell Volume (Chromium)	3.5–4.5	2.8–4.3	Per cent of Body Weight
Extracellular Volume (Thiocyanate)	20–25	20–25	Per cent of Body Weight

The measurement of total body water, total exchangeable sodium and total exchangeable potassium give us a very fundamental understanding of body composition which marks a very fortunate coincidence. The coincidence lies in the fact that Nature has given us readily available and readily usable isotopes to measure the three most important aspects of body composition and to calculate a fourth. Water, the body's solvent, the sea in which we swim, needs no introduction or apologia. The mass of potassium in the body represents the mass of lean oxidizing energy-exchanging tissue. The total exchangeable potassium seems to be directly proportional in size to the lean body mass and therefore constitutes our first direct measure of the total mass of oxidizing protoplasm. The total exchangeable sodium measures the "extracellular mass" if we can use that term. It is proportional to the amount of "stuff" which is outside of body cells. And fourthly, we can calculate from the total body water, the total body fat, by the formula developed by Pace:

$$\% \text{ fat} = 100 - \frac{\% \text{ water}}{.732}$$

This formula, based on the principle that lean tissue is 73.2% water, is merely a theoretical expression for the amount of fat in the body as related to the amount of water therein. Under stable conditions, and where acute disease is not involved, such an expression appears to be valid. By combining total body water measurements with metabolic balance and other experimental indices of this type, it is possible also to calculate the change in body fat directly.

We thus find that our three isotope dilution methods present us with a broad background picture of body composition in terms of water, cellular mass and extracellular mass. It will be interesting to see how these interrelationships are changed by disease.

The Depletion Syndrome

It is beyond the scope of this lecture to discuss in detail our findings in acute and chronic disease. We have been dealing with the story of the development of methods. However, it may be justified to pause a moment before closing and discuss findings which we have made in various types of depletion states.

In order to appreciate these, it is worth while considering what changes we might expect to observe.

First, as to body water. We can of course lose body water. Dehydration in the hot sun or from intestinal obstruction or from cholera all reduce our total body water. But it cannot be reduced very far, and all these reductions are very acute. If severe acute dehydration occurs it is incompatible with life beyond a certain point and there really is no such thing clinically as chronic dehydration. The amount of water which can be lost acutely is limited to

about 3–5 liters. Much more than five liters of acute dehydration is incompatible with life. We can therefore say at the outset that in studying chronically ill patients (who are not in the acute dehydrating phase of special diseases such as diarrhea or intestinal obstruction) we will not expect to see reductions in total body water. How about its increase? Here, quite the reverse is true. Body water is very easy to increase and it can maintain its increase for periods of many weeks or months. If we just drink too much water and salt we will find that our body water increases for many hours. And if there is liver disease or heart disease, physicians have known for years that edema forms and remains present for many months. So we would rather expect that we might find increases of total body water more frequently than decreases.

What about body fat? Without much further discussion, it is clear that chronic disease, especially if accompanied by any element of starvation, involves a reduction in body fat and this, too, would produce a relative increase in body water even if there were no absolute change in water content.

What about the lean body mass, the potassium-containing tissues? Here armchair reasoning would suggest that reductions were much commoner than increases. If we consider a normal healthy adult, there is only one way in which he can increase his total exchangeable potassium and that is by going into athletic training as a football player does, and increasing his muscle mass. Such of course does not occur in acute and chronic disease. Instead, we see the wasting away of muscle tissue so that we would predict that in chronic disease the total exchangeable potassium would tend to move in one direction, namely down.

And possibly the reverse would be expected to be true for sodium. Just as we can increase our total body water almost indefinitely, so also do we tend to increase our total body sodium, since the increases in body water, represented either by ascites or edema, are all sodium-containing water. So we would predict that in chronic disease sodium would change upwards more commonly than downwards, barring such specific agencies as Addison's disease or salt-losing nephritis.

Initial studies in chronically depleted individuals have indicated that these changes are the ones which are observed. The total body water tends to be relatively high and at times absolutely high in chronically ill individuals. The total amount of fat in the body is reduced. The total lean tissue mass, as measured by total exchangeable potassium, is low, and the total exchangeable sodium is high.

A wide variety of pathological conditions produce this depletion syndrome of altered body composition. It is seen in patients with advanced cancer, particularly involving the gastrointestinal tract. It is seen in chronic heart disease, chronic sepsis, chronic bowel disease such as colitis, and in the presence of chronic liver disease such as cirrhosis. In all of these conditions there is a wasting of body tissues, a shrinking of the lean tissue mass and expansion of the extracellular stuff represented by sodium.

If edema is present the exchangeable sodium is found to be much larger than under any other circumstances. General orders of magnitude for this depletion syndrome are as follows:

Total Body Water—As high as 75% of body weight.

Total Exchangeable Potassium—As low as 30 meq. per kilogram.

Total Exchangeable Sodium—As high as 65 meq. per kilogram where edema is present.

This depletion syndrome of altered body composition has very special meaning for the physician, and especially for the surgeon. When patients who exhibit this sort of change are traumatized either accidentally or by surgical operation, they tend very readily to develop marked water loading, hypoproteinemia, renal failure and cardiac decompensation. As a part of this post-traumatic change one commonly sees a low serum sodium concentration and a high plasma potassium concentration. Not very long ago this was referred to as "potassium intoxication", meaning that there was too much potassium in the body, and

"sodium deficiency", meaning that there had been a large loss of sodium.

Our efforts to track down these relationships between total body electrolyte and plasma concentration completes our story for tonight. In studying depleted patients preoperatively, we have often found that they maintained a low serum sodium concentration. Values in the range of 125 to 135 meq. per liter are quite common in these patients. It will be recalled that the total exchangeable sodium in depletion is usually normal or high. We therefore have our first paradox, namely, that the serum sodium concentration may be low at the very time that body sodium is high, and total body water even higher. So we are dealing in a sense with dilution of serum sodium by excess body water, as well as a possible redistribution of body sodium.

Turning to potassium we find that the opposite is true. The serum potassium tends to run at a high normal or definitely elevated figure in these chronically depleted patients. In our laboratories a serum potassium of 4.5 meq. per liter is on the high normal range. We see values of 5.0, 5.2 and 5.4 not infrequently in these chronically ill patients. And these values virtually always coexist with a low total exchangeable potassium. So our paradox is complete. Body sodium and potassium move inversely to each other, and the serum concentration of each ion tends in general to move inversely to the total body stores of that ion.

How might we explain this situation? We are not accomplished enough in matters of physical chemistry to conceive or investigate the defects in oxidative function or enzymatic transformation of energy which may be at the root of this. But it appears to us that it will be found to be based on variations in cellular energy level. Normal body cells require an abundant availability of caloric energy to maintain the concentration gradient across the cell surface which keeps potassium concentration high on the inside and low on the outside, and at the same time keeps sodium high on the outside and low on the inside. Energy is required both at the cell surface and in the renal tubule, to maintain this electrolyte concentration gradient. It is our theory that in a variety of chronically depleted states this energy level has fallen and the ability of the body to maintain the concentration gradient gradually falls. Just as depletion tends to increase body water and total sodium while the lean tissue mass wastes away, so also the deficit of energy results in a loss of the normal strong gradient-maintaining forces across the cell surface. We offer this theory with apologies since we can not prove it. It seems to fit the facts as far as we have observed them.

It has been said that we live in "ancient sea water"; the molar concentration of our extracellular fluid may resemble the sea water of many eons ago. Within this media of "ancient sea water" we have built up, as a result of vertebrate evolution and the available energy of each person, a very highly specialized mass of lean tissue which exchanges energy (and moves us around) and of neutral fat which stores energy. There are very few ways during our life in which we can build up further this mass of lean tissue. But in chronic depleting disease of many types, this mountain of lean tissue and fat tends to backslide into the ancient sea around us. We rarely can "climb up the ladder" of lean tissue dominance, but in many forms of disease, we slip backwards into our extracellular fluid, losing our muscle mass and fat, and losing our normal electrolyte relationships between cells and extracellular fluids.

Summary

The methods of tracer dilution in general, and of isotope dilution in particular, provide us with a means of measuring the total amount of certain body constituents in the living subject and thus of characterizing body composition. Methods and normal values have been described. A compositional syndrome characteristic of depletion has been outlined, and an interpretive theory suggested.

REFERENCES

Hevesy, G., and Hofer, E.: Elimination of water from the human body, Nature **134:** 879, 1934.

Crandall, L. A., Jr., and Anderson, M. X.: Estima-

tion of the state of hydration of body by amount of water available for the solution of sodium thiocyanate, Am. J. Digest. Dis. & Nutrition **1:** 126, 1934.

Cardoza, R. H., and Edelman, I. S.: The volume of distribution of sodium thiosulphate as a measure of the extracellular fluid space, J. Clin. Investigation **31:** 280, 1952.

Corsa, L., Jr., Olney, J. M., Steenburg, R. W., Ball, M. R., and Moore, F. D.: The measurement of exchangeable potassium in man by isotope dilution, J. Clin. Investigation **29:** 1280, 1950.

Edelman, I. S., and Moore, F. D.: Body water, water distribution and water kinetics as revealed by the use of deuterium oxide, J. Clin. Investigation **30:** 637, 1951.

Edelman, I. S., Olney, J. M., James, A. H., Brooks, L., and Moore, F. D.: Body composition: studies in the human being by the dilution principle, Science **115:** 447, 1952.

Edelman, I. S., Haley, H. B., Schloerb, P. R., Sheldon, D. B., Friis-Hansen, B., Stoll, G., and Moore, F. D.: Further observations on total body water. I. Normal values throughout the life span, Surg., Gynec. & Obst. **95:** 1, 1952.

Edelman, I. S., James, A. H., and Moore, F. D.: The location and the turnover of the sodium of bone. In: Reifenstein, E. C., Jr., *ed.* Metabolic Interrelations. Trans. Fourth Conference, p. 240. N. Y., Josiah Macy, Jr., Foundation, 1952.

Edelman, I. S., James, A. H., Baden, B. A., and Moore, F. D.: Electrolyte composition of bone and the penetration of radiosodium and deuterium oxide into dog and human bone, J. Clin. Investigation, *In press.*

Forbes, G. B., and Perley, A.: Estimation of total body sodium by isotopic dilution. II. Studies on infants and children; an example of a constant differential growth ration, J. Clin. Investigation **30:** 566, 1951.

Friis-Hansen, B. J., Holiday, M., Stapleton, T., and Wallace, W. M.: Total body water in children, Pediatrics **7:** 321, 1951.

Haley, H. B., Edelman, I. S., and Moore, F. D.: The turnover rate of body water in the human. In: American College of Surgeons. Surgical Forum, 1951, p. 595. Phila., Saunders, 1952.

Haley, H. B., Edelman, I. S., Frederickson, D. S., and Moore, F. D.: Water balance and electrolytes. The effect of thyroid disease on water turnover rate in the human subject. In: American College of Surgeons. Surgical Forum, 1952, p. 543. Phila., Saunders, 1953.

James, A. H., Brooks, L., Edelman, I. S., Olney, J. M., and Moore, F. D.: Body sodium and potassium. I. The simultaneous measurement of exchangeable sodium and potassium in man by isotope dilution, *In press.*

Moore, F. D.: Determination of total body water and solids with isotopes, Science **104:** 157, 1946.

Moore, F. D.: The use of isotopes in surgical research, Surg., Gynec. & Obst. **86:** 129, 1948.

Moore, F. D.: Radioactive isotopes in surgery, Surg., Gynec., & Obst. **92:** 372, 1951.

Moore, F. D., Haley, H. B., Bering, E. A., Brooks, L., and Edelman, I. S.: Further observations on total body water. II. Changes in body composition in disease, Surg., Gynec. & Obst. **95:** 155, 1952.

Moore, F. D., and Ball, M. R.: The Metabolic Response to Surgery. Springfield, Ill., Thomas, 1952.

Moore, F. D.: Bodily changes in surgical convalescence. I. The normal sequence: observations and interpretations, Ann. Surg. **137:** 289, 1953.

Moore, F. D.: The low sodium syndromes of surgery. An outline for practical management utilizing the DOCA test, J. A. M. A., *In press.*

Moore, F. D., Edelman, I. S., Olney, J. M., James, A. H., Brooks, L., and Wilson, G. M.: Body sodium and potassium. III. Inter-related trends in alimentary, renal and cardiovascular disease; lack of correlation between body stores and plasma concentration, *In press.*

Pace, N., and Rathbun, E. N.: Studies on body composition. III. The body water and chemically combined nitrogen content in relation to fat content, J. Biol. Chem. **158:** 685, 1945.

Pace, N.: Equations for the estimation of total body fat and total body water from the solubility of inert gases in the body. Rep. No. 4, Naval Med. Res. Inst., Bethesda, Md., 1945. Research Project X-191.

Schloerb, P. R., Friis-Hansen, B. J., Edelman, I. S., Solomon, A. K., and Moore, F. D.: The measurement of total body water in the human subject by deuterium oxide dilution; with a consideration of the dynamics of deuterium distribution, J. Clin. Investigation **29:** 1296, 1950.

Schloerb, P. R., Friis-Hansen, B. J., Edelman, I. S., Sheldon, D. B., and Moore, F. D.: The measurement of deuterium oxide in body fluids by the falling drop method, J. Lab. & Clin. Med. **37:** 653, 1951.

Solomon, A. K., Edelman, I. S., and Soloway, S.: The use of the mass spectrometer to measure deuterium in body fluids, J. Clin. Investigation **29:** 1311, 1950.

Wilson, G. M., Edelman, I. S., Brooks, L., Myrden, J. A., Harken, D. E., and Moore, F. D.: Metabolic changes associated with mitral valvuloplasty, *In press.*

Wilson, G. M., Olney, J. M., Brooks, L., Myrden, J. A., Ball, M., and Moore, F. D.: Body sodium and potassium. II. A comparison of metabolic balance and isotope dilution methods of study, *In press.*

The Vanishing Spas of Pennsylvania (An Historical Review)*

By IGHO H. KORNBLUEH†, M.D., AND GEO. MORRIS PIERSOL‡, M.D.

PART II

Huntingdon Warm Spring[1]*—Huntingdon County*

Huntingdon Warm Spring, five miles from Juniata College, once played an important part in the settlement of central Pennsylvania. Diaries and travelogues of Rev. Philip Fithian of Greenwich, New Jersey, were used extensively by two local historians, Africa (31) and Rung (32). Reverend Fithian, attracted by the reputation of Huntingdon Warm Spring, visited it on August 22, 1775. He found there 22 persons seeking health and recovery, and "barren women" hoping for pregnancy. The people were "living in log cabins built with slabs and boughs". Interesting are his observations on the spring. "The water rises boiling up with sand and much air in bubbles . . . is quite clear . . . has no unusual odor or taste and is not indeed cold. I think it like some springs which I have seen running without a shade in summer." It was assumed at that time that the healing powers of this water were known to Indians, who came here from great distances, and later to early settlers from Virginia.

The first tavern in Huntingdon Warm Springs was probably erected by John Fee in the beginning of the 19th Century. Rung quotes an advertisement in the Huntingdon Gazette of June 27, 1811 signed by Israel Evans, then operator of this tavern, which states: . . . "He has put the Very Old Bath House in a complete state of repair and intends immediately to erect a new one . . . either for the benefit of their [the guests'] health or person. He has also supplied himself with a good stock of liquors, etc.", a perfect combination for a successful spa of that era.

In February, 1844, Joseph Forrest, one of the later proprietors of Warm Springs, quoted in an announcement an account of the properties of this spring by Dr. Thomas Duncan Smith, from the *Huntingdon Literary Museum* of 1810. Dr. Smith, "An able and scientific physician", had the following to say of the waters: ". . . Specific gravity exactly that of pure rain water, the taste is soft and smooth, the temperature 64°F. . . . The use increases perspiration, acts gently on the bowels and freely on the kidneys . . . they promote appetite and restore it to those who have long labored under its loss." Col. William Dorris acquired the Warm Springs property previous to the Civil War and sold it shortly afterwards to a Porter Wilson, a successful attorney, who attempted in turn to sell Warm Springs to the Pennsylvania Railroad.

The competition of Bedford Springs was probably responsible for the financial failure of the Huntingdon Warm Springs Hotel, which was closed before 1876. No trace of the hotel building was found. A circumwalled spring

* Read in part before the College of Physicians of Philadelphia, Section on Medical History, 29 January 1953. Part I appeared in the *Transactions & Studies* 4th s. **21:** 63–77, August, 1953.

† Instructor in Physical Medicine and Rehabilitation, Graduate School of Medicine, University of Pennsylvania; Chief, Department of Physical Medicine and Rehabilitation, Northeastern Hospital, Philadelphia.

‡ Professor of Medicine, Chairman, Department of Physical Medicine and Rehabilitation, Graduate School of Medicine, University of Pennsylvania, Philadelphia.

[1] We are indebted to Mr. Morley Mays, Dean of Juniata College; the late Norman J. Brumbaugh, D.Sc., Ph.D., Professor Emeritus of Juniata College; and Floyd G. Hoenstine, of Hollidaysburg, for their cooperation and help.

and the remnants of a large pool are all that remain of this spa. The temperature of the spring, taken in the summer of 1952, was 13.5°C. (56.3°F.), well below the 64°F. mentioned by Smith. No signs of "boiling" (escape of gas) as mentioned by Rev. Fithian were present. The surrounding grounds are infested with rattlesnakes and the location of the spring is known to only a few of the older inhabitants of Huntingdon.

Kiskiminetas—Indiana County

Kiskiminetas spring is situated on a lofty hill, overlooking Saltsburg and the surrounding country. It had a stately hotel, built on the reputation of its three springs, iron, magnesia and a pure water spring, said to have existed there on the slope of the hill. Erosion has succeeded in covering these springs with earth and stones. Only the critical eye of the Professor of Mathematics and Assistant to the President of the present school, Mr. R. K. Brinker, could discern the location of the springs. The hotel was constructed in about 1875 and sold in 1888 to A. W. Wilson, Jr., who in turn established a private school here. Kiskiminetas, the Indian "dawn of the day", was used for some time as a watering place during the vacations, even after the founding of the school. Today, Kiskiminetas, with its motto, "Humility—Faith—Tolerance", is one of the leading Pennsylvania prep schools, accentuating both general education and, as befits a former spa, physical and health programs as well.

The former hotel is now called "Old Man", the central building of a large campus. The tradition of Kiskiminetas as a successful spa still lingers in the memories of the older members of the teaching staff.

Ligonier—Westmoreland County

In this western Pennsylvania community, around an old magnesia spring, a spa was developed which prospered for a number of years. The construction of Kissel's Spring Hotel in the later 50's of the 19th Century provided the summer guests with adequate accommodations. A new and better hotel followed in 1880. Modernized and rejuvenated, it is well known today to travelers as Fort Ligonier Hotel. These changes in the buildings failed to affect the spring or to alter nature's perpetual laws.

Loganton—Clinton County

The sulphur spring at Loganton is situated about 80 miles northeast of Altoona and some fifteen miles from Lock Haven. Known for the past hundred years, the water of the spring was held in high regard for its therapeutic qualities. The very low output of the spring must have tried the patience of those who attempted to collect its water in large jugs. A penetrating smell of rotten eggs emanating from this water is probably still attractive to some people, who believe in its efficiency. Mr. W. E. Meyer, Vice-President of the Loganton National Bank, is well acquainted with the medicinal properties of this spring. Kept in good condition and well protected by an attractive spring house, it served in the past the summer guests of a hotel known as the Logan House. Built long before the turn of the century, the hotel burned down in 1918 and no attempt was ever made to replace it.

McElhattan[2]—Clinton County

McElhattan Springs, East of Lock Haven, on the West Branch of the Susquehanna River, attracted many visitors during the summer season. The water supply came from five individual springs. Accommodations for the guests were provided by several hotels in the vicinity. The "medicinal" waters were used for drinking and bathing. Baths were taken in the bedrooms in portable wooden bathtubs. A local trout hatchery was another great attraction. The therapeutic value and the mineral properties of McElhattan's springs were never established.

[2] We are grateful to Henry W. Shoemaker, of the Pennsylvania Historical and Museum Commission, for this information.

Minnequa Springs—Bradford County (Vicinity of Canton)

History, folklore, and the tradition of Minnequa Springs (33, 34), in the vicinity of Canton, are still vivid, thanks to the interest displayed by a number of citizens of this community. The spring, known as the "Indian Healing Spring", was discovered by white men before 1771. The local lore relates the story of Minnequa, the beautiful daughter of an Indian Chieftain, who made a miraculous recovery from a deadly disease, after drinking water from the magically healing spring (35).

Another legend tells of an elaborately dressed stranger, who came over the mountains to quench his thirst at the Indian Spring. It is said that the magic water made him grow without affecting his health. The "Giant of Minnequa" died at a very old age and his neighbors had great difficulty in burying his oversized body.

In 1868, Peter Herdic acquired the spring and the surrounding grounds, after obtaining relief from a rheumatic condition by the use of its water. The first hotel, erected by Herdic in 1869, accommodated 600 guests. The spring was protected against contamination and covered by an open spring house. The first Minnequa Springs Hotel burned down in 1878. It was followed by another hotel. This wooden building, smaller than the first, with a porch facing the railroad track, was closed in 1901 and two years later destroyed by fire. The hotel had only 92 bedrooms in the main building and 36 additional rooms in an annex near the spring. Two cottages nearby with 14 bedrooms increased the total capacity to about 300 guests. The spring and the Victorian springhouse are well preserved and easily accessible. An old description of the spring lists the following medical indications: "Keeps blood and excretions alkaline; increases metabolism and promotes tissue repair; enhances the action of the saliva, bile, and intestinal juices; aids in the change of gases in the tissue and lungs, by acting as a carbonic acid carrier; is indicated in dyspepsia, constipation, gall stones, gravel, gout, diabetes, skin eruptions, rheumatism, neuritis, and obesity.

The present owner of the spring, Mr. William Spencer Castle, Sr., has in his possession the following chemical analysis of Minnequa Spring, made by the Pittsburgh Testing Laboratory on December 5, 1936, laboratory # 188736, file # 11992.1, order # page 15180, marked David E. Fisher and signed by H. H. Craver.

Free carbon dioxide	25.00 p/m
Iron oxide	2.86 p/m
Calcium carbonate	99.68 p/m
Magnesium carbonate	25.66 p/m
Sodium carbonate	Trace p/m
Lithium carbonate	Trace p/m
Calcium sulphate	0 p/m
Magnesium sulphate	Trace p/m
Sodium sulphate	33.16 p/m
Calcium chloride	0 p/m
Magnesium chloride	Trace p/m
Sodium chloride	9.90 p/m
Manganese	0.50 p/m
Silica	2.00 p/m
Alumina	1.89 p/m
Total solids	174.00 p/m

Monterey—Franklin County

Monterey Springs Hotel, located in the vicinity of Monterey Peak of the Blue Ridge Mountains, was one mile north of the Blue Ridge Station of the Western Maryland Railroad. The hotel, a three-story building, with many dormers and a fountain in front of the hotel, existed in Monterey about 1850. A Mr. V. P. Holmes acquired this hotel and after complete renovation and the addition of modern facilities, including hot and cold baths, reopened it in August, 1877. In an advertisement of the same year the proprietor had the following to say: "In the years 1875–76, this hotel, with its meagre accommodations was crowded to excess, and turned away over 1000 applicants for want of room". Holmes stressed the mountain scenery, mineral and medicinal waters, containing iron, magnesia, and sulphur, the freedom from mosquitoes, and moderate temperatures because of an elevation of about 2500 feet. Interesting are the terms quoted in the same

leaflet: "$2.50 a day, table board, $7.00 per week, rooms $3.00 per week and upward, depending upon the length of stay, children and servants by special contract."

A stop at Mount Summit will convince the visitor that even today many claims made by V. P. Holmes are correct. Changes in the last 76 years were certainly not to its disadvantage. A charming family resort at an elevation of 1365 feet, Monterey has much to offer and remains a restful place for both the eyes and souls of all people who have not lost their admiration for natural beauty and grandeur. At Monterey, many hotels catered to summer guests at different periods but none have been able to survive the changes wrought by time and growing public indifference. One after another they disappeared. The Springs Hotel went up in flames in July, 1942.

A short distance from Monterey is another lovely spa, Buena Vista, once famous for the excellence and reputation of its springs.

Mount Holly—Cumberland County

At Mount Holly, situated in a deep valley along a mountain creek, there are a number of springs. The one spring situated in the southern part of the valley was bottled about twenty years ago. A still existing hotel was once used as a resort hotel. It seems that Mount Holly never acquired any great significance as a watering place.

Perry Warm Springs—Perry County

Situated in the vicinity of Alinda, at the foot of the Pisgah Mountain on the banks of Sherman's Creek, Perry Warm Springs is listed by the Geographical Survey of the United States Department of the Interior (36) as the only thermal spring in Pennsylvania. The following description is found in the Geological Survey: "Near Shermansdale, fifteen miles northwest of Harrisburg; folded Paleozoic rocks, temperature 72°F., approximate discharge 90.0 gal/pm, formerly a hotel; water bottled. It was early developed as a bathing resort, but in recent years it has not been so used. The temperature indicates that the water rises from a considerable depth."

Bell (18) describes the location of Perry Warm Springs as follows: "On the banks of Sherman's Creek, eleven miles from Carlisle, fourteen miles from Harrisburg, and at the same distance from Duncannon at the foot of the Pisgah Mountain." It was rather difficult to find this unique spring and the Warm Springs Hotel, a wooden structure of 2½ floors, with a ground floor of stone. A rotting porch at the height of the second floor, runs half way across the front of the hotel. It is more than 100 years old and in deplorable condition, but still partly inhabited. Its function as a spa was abandoned before the beginning of the century. At a distance of a few hundred feet across a dirt road, bedded in high grass and camouflaged by trees is the thermal spring. A high, slightly circular wall, built of perfect rectangular stones, protects the spring from the roadside. Below the center of the wall, at the foot of two ancient oaks lies the spring. Underneath a turbid surface, there is a clear, odorless water draining to Sherman's Creek. A check on the temperature of the water disclosed a slightly lower temperature than that reported by the United States Geological Survey.

According to local history and an old picture of the original hotel and the surrounding grounds, guests enjoyed here the healthy and clean air of old coniferous forests, boating, and other activities, besides the main attraction: thermal water. The waters were used internally at the spring and for baths administered in a small bath house near to the hotel. Smaller than the bath house at Huntingdon, it featured, in two separate sections, natural cold and warm baths.

Pulaski—Lawrence County

Pulaski Springs, near the western border of Pennsylvania, underwent two distinct periods, first as a spa and then as a bottling place of mineral water.

An old spring or well was located close to the town, on the east side of the Shenango River. It was known since 1866 and used extensively for therapeutic purposes. The spa of Pulaski had two hotels, only a short distance apart. One hotel accommodated a few hundred guests and dispensed mineral water, containing iron, from a well adjacent to the hotel. Hot mineral baths were available in a special bath house.

The other hotel was much smaller and catered only to summer guests. It was permanently closed around 1912.

The nemesis of the great majority of the spas of Pennsylvania did not spare Pulaski. Both hotels were destroyed by fire in 1916. The source of the mineral waters could not be located.

On the western side of the Shenango River there is a relatively new mineral well of the considerable depth of 500 feet. It was discovered accidentally in 1888 by companies drilling for oil and gas. This water was bottled until 1943. During World War II, the pump and other machinery were removed and, up to the present time, have not been replaced. The owners, S. N. and G. H. Garfunkel, residing in Farrell, supplied the following analysis:

Analyzed August 15, 1938 by F. C. Buckmaster, Chemist, Pittsburgh, Pennsylvania:

Magnesium carbonate	2.486	g/gal
Silica	0.232	g/gal
Iron and alumina	0.464	g/gal
Potassium chloride	2.016	g/gal
Sodium chloride	263.87	g/gal
Lime carbonate	15.428	g/gal
Organic matter	None	g/gal
Total solids	284.496	g/gal
		(= 4.870 p/m)
Free carbonic acid gas	0.574	g/gal

"This is a water of great organic purity, which possesses the highest qualities as a beverage, but also contains minerals in such combination as to give it a very decided medicinal value."

A more recent analysis, made by Creig S. Hoyt, Thiel College, Greenville, Pennsylvania, April, 1945, is as follows:

Alkalinity to phenolphthalein	0	p/m
Alkalinity to methyl orange	369	p/m
Free carbon dioxide	10	p/m
pH	7.6	p/m
Hardness by soap solution	2783.	p/m
Hardness calculated	317	p/m
Lithium	Trace	p/m
Calcium	86.8	p/m
Magnesium	22.2	p/m
Iron	2.4	p/m
Alumina	31.5	p/m
Alkalies	1920.	p/m
Silica	8.5	p/m
Chlorides	2911.0	p/m
Sulphates	1.8	p/m
Total solids	4984.2	p/m

Hypothetical Compounds

Ferrous bicarbonate	7.65	p/m
Calcium bicarbonate	351.00	p/m
Magnesium bicarbonate	134.00	p/m
Lithium bicarbonate	Trace	p/m
Sodium bicarbonate	100.00	p/m
Sodium sulphate	2.60	p/m
Sodium chloride	4730.00	p/m
Potassium chloride	39.00	p/m
Silica	8.5	p/m
Alumina	31.5	p/m

Saegerstown—Crawford County

In the northwestern part of the State, about midway between Cambridge Springs and Meadville, is Saegerstown. In the center of the town are the ruins of two resort hotels with bath and spring houses. In reality, the "medicinal" water did not come from springs, but from a well, drilled there in 1883. In ensuing years, additional mineral wells were opened.

This water, having a peculiar taste, was analyzed at Allegheny College in the summer of 1884 (37). It was found to contain rather large amounts of iron and magnesia. The Benner Brothers erected a bath and a spring house and also exploited the water commercially. The bottling plant was known as Eureka Springs and later as the Saegerstown Mineral Water Company. In 1886, Ira Fuller, a man of means, built a three story hotel on

Main Street, known as Arlington. Destroyed by fire in September, 1887, it was partly rebuilt the following year. A new hotel, the Old Inn, was constructed shortly afterwards nearby. An amusement park, dance pavilion, and picnic grounds were situated on the opposite shore of French Creek. Even a museum was added in a park south of the Inn. A steamer called the "Valley Queen" took hotel guests for short rides on French Creek.

In 1929, Dr. Burchfield, of Titusville, acquired the Old Inn, only to close and dismantle it some four or five years later. All that remains of the Old Inn are the floor of the ball room and parts of the walls. The original well is no longer used. Above the old fireplace, which is being preserved as an historical marker, is the following inscription: "I am an old man and have had many troubles, but none of them ever happened."

A real effort was made to create in Saegerstown a modern and comfortable spa with diversions and amusements fitting well into the concepts of such therapy. The existence of such a flourishing place as Cambridge Springs, only a few miles distant, may have been a contributing cause of its final failure.

Sizerville—Cameron County

The unusual taste or smell of a water has been regarded in the past as a potential therapeutic and financial asset. Such mineral water was used for drinking as well as bathing at the wooden and primitive sanitarium at Sizerville. Here bath prices varied according to demand; they ranged up to $5.00.

A 180 foot deep artesian well, drilled in 1899, supplied the water for this "health institution" and a bottling plant. The sanitarium, erected about 1899, was torn down in 1912. For a time, Sizerville attracted many sick people hoping for recovery as the result of using the water. Even after the discontinuance of hydrotherapy, bottled water was sold there for fifty cents a quart.

Part of the foundation of the sanitarium is still visible. The water of the artesian well is now used by Mr. Jack Hanes for domestic purposes. There is a local belief that another spring closer to the railroad is even more effective for certain ailments than the original well.

Three Springs—Huntingdon County

At Three Springs, known formerly as Scottsville, there were a few springs, but only one was used extensively for medicinal purposes. This main spring, in close vicinity to the firehouse, is well preserved but of low output. The water of this spring was used internally over a period of many years. The town had at different times two hotels, both still in good condition. The larger one, on Main Street, dates back to the second half of the last century. Closed before 1900, it is now used as a private dwelling. A block farther on, close to the post office, is a small house which once served as a hotel for people who came to Three Springs hoping to find relief from their afflictions by the use of its reputed waters.

G. G. Pond analyzed spring number 1 with the following results:

Sodium chloride	5.98 p/m
Lithium sulphate	0.34 p/m
Potassium sulphate	Trace p/m
Sodium sulphate	101.06 p/m
Magnesium sulphate	573.53 p/m
Calcium sulphate	926.79 p/m
Calcium bicarbonate	941.86 p/m
Silica	19.68 p/m
Total solids	2569.24 p/m

Gases

Carbon dioxide	18.8 cc/liter
Oxygen	5.9 cc/liter
Nitrogen	13.3 cc/liter

Tuckhoe Mineral Springs—Northumberland County

Situated about a quarter of a mile off Route 11 and well hidden by old trees, is a small resort called Tuckhoe Mineral Springs. A number of cottages and a good-sized swimming pool formed the nucleus of a spa, which has outlived its popularity. Well known at the turn of this century as the site of the Tuckhoe Lithia Spring Company, it has three

mineral springs: (a) lithia, (b) magnesia, (c) sulphur. All three springs are located within a small area only a few hundred feet apart. Tuckhoe Mineral Springs suffered the fate of the "Flying Dutchman", legally dead, due to contamination of its springs; it uses its water for the swimming pool only. The bottled water of the Tuckhoe Mineral Springs Company was widely distributed some fifty years ago. It is alleged that the company artificially increased the contents of lithium in the water, seemingly without any harm to its regular users. An old undated and unsigned analysis, in the possession of Mr. L. H. Mertz, the present owner of Tuckhoe, shows the contents of the Lithia Spring:

Magnesium sulphate	1.2500	gr/gal
Magnesium carbonate	2.4700	gr/gal
Sodium chloride	6.2100	gr/gal
Potassium chloride	4.0500	gr/gal
Potassium carbonate	0.0027	gr/gal
Calcium carbonate	3.2800	gr/gal
Sodium bicarbonate	12.4503	gr/gal
Magnesium carbonate	1.4200	gr/gal
Lithium bicarbonate[3]	4.1116	gr/gal
Alumina phosphate	Trace	gr/gal
Organic matter	None	gr/gal
Total solids	35.2446	gr/gal

Despite a statement in an old pamphlet that "hundreds" of people far and wide can testify to its (medicinal) value . . .", Tuckhoe remains, as a watering place, a modern anachronism.

York Sulphur Spring—Adams County

York Sulphur Spring was once a well known spa. Older than the spa of Gettysburg, it was, according to Dr. H. Stewart, also of greater social significance, especially in the last two decades of the 19th century. Between 1850 and 1900, the York Sulphur Spring Hotel faithfully served two generations of satisfied guests. It suffered the same fate as most of the other resort hostelries, burning down about the beginning of this century. The stones from the original hotel were used for the residence of Mrs. Gardiner, the present owner of the spring. The spring, on the right bank of the Bermudian Creek, is three quarters of a mile from the intersection of routes 95 and 15, southeast towards Hanover.

Bedford

On the outskirts of the town of Bedford there was a famous hotel, the Bedford Chalybeate Springs Hotel, situated close to the Pennsylvania turnpike. The property was purchased by George Funk in October, 1786, and called "Funk Spring". Shortly afterwards, the new owner erected the first hotel, which was enlarged by permanent structures in 1805, 1855, and 1888. A large ballroom was added in 1892. The water from Chalybeate Spring was used by the guests for drinking only. An 800-foot long wooden boardwalk connected the hotel with the spring. Warm baths in lime-water were available in a special bath house close to the hotel. On June 12, 1888, G. H. Dauler announced the completion of "a new brick addition, large spacious dining room, ordinary bath rooms and other out buildings for the convenience of guests."

Twenty years later, the therapeutic value of this spring was stressed by Dauler: "The Chalybeate waters are unsurpassed for their curative powers in ailments of the stomach, liver and kidneys."

Chalybeate Springs Hotel was closed in 1912 and some years later sold to Mr. and Mrs. E. Ernest Buterbaugh, who re-opened it in 1947. Closed again as a resort in 1950, it serves now as a spacious private dwelling.

In the original guest book may be found a number of famous names: Benjamin Harrison, Horace Greeley, J. Gould, C. Vanderbilt, and many others of more or less prominence. The buildings and the spring are well preserved and easily accessible.

An ointment, at one time extensively used, was composed by one Hafer from the "sediment drawn out of the famous Bedford Chalybeate Springs." This preparation was known as Hafer's "Celebrated Chalybeate Cure", a specialty for skin diseases and piles, registered in 1887.

[3] Concerning Lithium, there are some well founded doubts about the accuracy of this figure.

According to Hafer's statement, this ointment, which sold for ten cents, was "More commonly known as iron salve." It was recommended as a "specific for the following diseases"—piles, teeter, eczema, salt, rheum, prurigo, milk crust, itching piles, ivy poison, etc.

The leaflet on Hafer's salve contains the following analysis of the Chalybeate water:

Carbonate of calcium	201.1730 p/m
Carbonate of magnesium	37.0810 p/m
Carbonate of iron	7.4927 p/m
Carbonate of sodium	14.4750 p/m
Carbonate of potassium	3.8801 p/m
Sulphate of calcium	70.6271 p/m
Phosphate of calcium	2.3273 p/m
Chloride of sodium	2.1667 p/m
Silicic acid	12.2000 p/m

The Surviving Resorts

At the present time, there are only three locations in which flourishing health resorts still exist—Bedford Springs, Cambridge Springs, and White Sulphur Springs. It is appropriate, therefore, to consider these resorts in a separate group.

Bedford Springs—Bedford County

Situated in a beautiful valley amidst foothills of the Allegheny Mountains, 1500 feet above sea level, Bedford Springs has a mild, equable and salubrious climate.

Tradition says that tribes of Tuscaroras and Iroquois held their conclaves in a wondrous glen around a "medicine spring, four days' journey from the mighty ocean toward the setting sun."

Bedford Springs' waters were known, appreciated, and revered by the red men centuries before the advent of the Europeans in this country.

The discovery of mineral springs at Bedford in 1796 is ascribed to Nicholas Schouffler (32), who found them accidentally while prospecting for gold. A few years later, about 1804, as the result of a reported cure of a mechanic of Bedford suffering from "rheumatism and formidable ulcers of the leg", the fame of these waters spread rapidly throughout the east, thereby attracting thousands of visitors yearly. Bedford Springs (38, 39, 40) may be classed as one of the oldest, largest and most famous watering places in this country. Gordon's Gazetteer mentioned Bedford Springs as early as 1804 and then again in 1832.

The first hotel, of several to be erected at Bedford Springs, was opened to the public in 1817. It was a stone structure four stories high. It was enlarged in 1884 by a more elaborate building, which underwent repeated improvements. The old buildings were retained and a new modern structure, an elegant fireproof building was added in 1924. Here the recreations available include golf, tennis, horseback riding, and swimming in a covered pool.

The Bedford "cure" has been used with reputed success in the following chronic disorders: gout and the gouty diathesis, chronic rheumatism, rheumatic and gouty arthritis, autointoxication, chronic constipation, intestinal stasis, chronic catarrhal disorders of the liver, gall bladder, kidney insufficiency, albuminuria, neurasthenia, hypertension and obesity. After Bedford became known as "The Carlsbad of Pennsylvania", it attracted many persons suffering from gastrointestinal, biliary tract, and renal diseases.

Bedford has four different mineral springs, of which the magnesia spring is undoubtedly the most valuable. It is still used extensively by the hotel guests. The use of the sulphur spring was lately discontinued. The experience and knowledge of its former medical director, Dr. Fitch, has greatly contributed to the better therapeutic application of these existing natural resources.

The medical indications for the uses of Bedford Springs water have been renal insufficiency, diabetes, various gastro-intestinal ailments, and diseases of the gall bladder.

An analysis of the water from the Magnesia Spring is as follows:

Hypothetical Combinations

Ammonium chloride (NH_4Cl)	0.6 p/m
Lithium chloride ($LiCl$)	Trace p/m

Potassium chloride (KCl)	3.6 p/m
Sodium chloride ($NaCl$)	4.4 p/m
Potassium iodide (KI)	Trace p/m
Potassium sulphate (K_2SO_4)	Trace p/m
Sodium sulphate (Na_2SO_4)	13.7 p/m
Magnesium sulphate ($MgSO_4$)	703.0 p/m
Calcium sulphate ($CaSO_4$)	1650.0 p/m
Strontium sulphate ($SrSO_4$)	Trace p/m
Calcium phosphate ($Ca_3(PO_4)_2$)	—
Sodium bicarbonate ($NaHCO_3$)	—
Magnesium bicarbonate ($Mg(HCO_3)_2$)	—
Calcium bicarbonate ($Ca(HCO_3)_2$)	267.3 p/m
Strontium bicarbonate ($Sr(HCO_3)_2$)	Trace p/m
Ferrous bicarbonate ($Fe(HCO_3)_2$)	—
Manganese bicarbonate ($Mn(HCO_3)_2$)	—
Ferric oxide and alumina (Fe_2O_3, Al_2O_3)	3.0 p/m
Calcium silicate ($CaSiO_3$)	45.7 p/m
Silica (SiO_2)	—
Total Solids	2691.3 p/m

Gases

Carbon dioxide (free) per liter	8.9
Carbon dioxide on evap. to dryness, c.c. per liter	36.7
Hydrogen sulphide, c.c. per liter	2
Temperature, C.	14.4
Flow in gallons per day	24,000

Today Bedford Springs is not thought of so much as a spa as it is a popular resort. The spacious modern accommodations available and its attractive surroundings have earned for it a reputation as an ideal location for large meetings and conventions.

Cambridge Springs—Crawford County

A pleasant resort town, Cambridge Springs boasts of five mineral springs at various locations; a boarding house (Chadwick's Lithia Spring) and a large convalescent home (San Rosario) are at one end of the town, while a large hotel (the Riverside Inn) and the "original magnesia spring" are at the other end. The so-called lithia water of Chadwick's Spring was used therapeutically by guests of the boarding house and others. San Rosario, built originally as a hotel before the 1929 depression, is now owned by a Catholic order and conducted as a modern home for convalescents.

Mr. Michael Kalaidzic, a highly skilled wood carver, owns the "original magnesia spring." Not interested in any commercial exploitation, Mr. Kalaidzic uses the mineral water solely for domestic needs, but keeps the grounds and the large fountain house in excellent repair. Analyzed more than half a century ago, by J. H. Montgomery of Allegheny College, the water was recommended for dyspepsia, stomach, liver, kidney, and other diseases. Albuminuria, gout, rheumatism, insomnia, indigestion, torpid liver, and loss of appetite are said to have responded well to this water. "It is not an actual cathartic, but is the only combination diuretic, tonic, and laxative water prepared by nature . . . the satisfactory results following the use of this water have caused it to become famous without the aid of any other advertising agency."

It contained, according to Montgomery, iron carbonate, calcium bicarbonate, magnesium bicarbonate, sodium chloride, etc. He classified it as "A mineral water of high order". Another analysis, made by the Allegheny College Chemical Laboratory at Meadville, Pennsylvania on February 24, 1925, signed by R. E. Lee, Sc. Dr., showed the presence of the following chemical combinations:

Magnesium bicarbonate	53.6 p/m
Calcium bicarbonate	206.1 p/m
Sodium sulphate	8.1 p/m
Iron bicarbonate	10.9 p/m

"Chemical analysis showed this water to be a highly mineralized magnesia bicarbonated water of the alkaline type. Approximately 82 per cent of the solids in solution are in the form of bicarbonate of magnesium and calcium, with 3 per cent of sodium sulphate, and 4 per cent of bicarbonate of iron. Such waters as this act as a mild laxative and are perhaps the best of all the carbonated alkaline waters in correcting an acid condition of the stomach. They favor the solution of uric acid, are valuable agents in breaking up deposits in the bladder, and are much used in catarrhal conditions of the mucous membranes of the urinary organs."

An enterprising local physician, Dr. J. H. Gray, while prospecting for oil in 1859, discovered an iron spring and used it for medicinal purposes. A second spring, the magnesia spring, was found in the same vicinity some years later.

In 1889, a small resort hotel, Riverside Inn, was erected in the vicinity of the Gray Spring. In 1895 this property was acquired by William Baird. A casino for amusement, a bath house, an elevated boardwalk leading to Gray's Spring were added. The greatly enlarged and modified Riverside Inn remained in the possession of the Baird family for 51 years. A company headed by Col. Francis W. Parke purchased Riverside Inn in 1946. Modern, excellent accommodations and recreational facilities attract many guests. The hotel features two kinds of mineral water, iron and magnesia, which are different in character and taste. The latter is piped directly to the Inn and used as drinking water in the dining room, while the iron water is dispensed at the restful spring house.

We are obliged for the analyses of both springs to Col. Francis W. Parke, President of the corporation.

Gray's Mineral Spring analyzed by John A. Miller, Ph.D.:

Potassium chloride	0.1141 g/gal
Sodium chloride	0.1999 g/gal
Sodium sulphate	0.2421 g/gal
Sodium bicarbonate	1.1307 g/gal
Ferrous bicarbonate	0.9155 g/gal
Calcium bicarbonate	7.5705 g/gal
Magnesium bicarbonate	2.6049 g/gal
Silica	0.7788 g/gal
Alumina	0.1597 g/gal
Phosphoric acid	Trace g/gal
Arsenic	Trace g/gal
Total solids	13.7162 g/gal (234.71 p/m)

"This water is organically pure. It is antacid, diuretic and tonic in its character."

Magnesia Water

Sulphuric acid radicle	5.5 p/m
Bicarbonate acid radicle	89.6 p/m
Chloride	4.0 p/m
Iron	7.2 p/m
Alumina	1.0 p/m
Calcium	20.0 p/m
Magnesium	5.2 p/m
Total solids	132.5 p/m

Hypothetical Compounds

Ferrous bicarbonate	23.6 p/m
Magnesium chloride	5.4 p/m
Magnesium sulphate	6.9 p/m
Magnesium bicarbonate	15.3 p/m
Calcium carbonate	80.3 p/m
Alumina	1 p/m
Total solids	132.5 p/m

White Sulphur Springs, P. O. Mann's Choice—Bedford County

A short distance from Bedford is an active, beautifully situated spa, White Sulphur Springs. Long before the construction of a permanent hotel, White Sulphur Springs had a log building serving as an inn for summer guests. This Inn was very popular for many years. In 1886 a new hotel, built by a Mr. Colvin, the White Sulphur Springs Hotel, replaced the old house and inaugurated a new era of comfort not previously experienced by visitors. A Sulphur Spring, famous for its therapeutic results, was its main attraction. The conversion of this building to a luxurious resort for convalescents, chronically ill, and vacationists, by its present owners, Mr. and Mrs. Paul B. Cochran, is an excellent example of free American enterprise. The hotel was recently completely rebuilt, tastefully refurnished, and modernized.

History has it that the Shawnee Indians knew and believed in this spring. A Shawnee trail on the property, and relics of the tribe, prove that the water was known to them long before white men settled in central Pennsylvania. It is interesting that White Sulphur Springs was referred to in the same issue of an early Pennsylvania newspaper which reported an interview with Napoleon Bonaparte, then interned on St. Helena.

As an all year round resort, White Sulphur Springs also features many elaborate attractions for active and healthy guests. The extremely low incidence of hay fever makes this region very desirable to sufferers whose

allergic manifestations are due to ragweed and related pollenosis. Convalescents, hypertensives, and persons with chronic heart disease in a stage of full compensation, will find White Sulphur Springs a restful place, with level walks and the environment helpful in the management of such conditions.

The crystal clear spring provides excellent water of moderate mineralization. The analysis by F. A. Genth of the University of Pennsylvania, performed some years ago, discloses the presence of the following chemical combinations:

Lithium chloride	Trace p/m
Sodium chloride	3.29 p/m
Sodium sulphate	17.10 p/m
Potassium sulphate	3.70 p/m
Calcium sulphate	6.08 p/m
Magnesium sulphate	16.78 p/m
Calcium sulphate	Trace p/m
Calcium bicarbonate	154.63 p/m
Magnesium bicarbonate	22.03 p/m
Ferrous bicarbonate	11.29 p/m
Silica	30.96 p/m
Total solids	263.86 p/m

With the exception of a few persons, who, proud of the past of their home towns could supply some interesting information, our younger generations grew up in complete ignorance with regard to events so highly cherished by their elders. For the superficial reader, the description of Pennsylvania's spas will have only historical significance. Persons interested in balneology or those who carry the responsibility for an improvement of our too scarce resorts might find here some pertinent information. Pennsylvania has in many respects much more to offer than is generally known. The generosity of nature and the heavy toil of many generations converted this blessed piece of land into one of the most beautiful and restful in the western world. The hope that the Keystone State will outgrow an observation made by Disturnell (40) nearly a century ago, and, overcoming its lethargy, awaken to its vested obligation, will never vanish.

Conclusions

A survey such as the one herein reported furnishes convincing evidence of the decline and virtual elimination of all but three of the spas and watering places in the State of Pennsylvania, over the last seventy-five years. Such a situation is not peculiar to that State; it is nationwide in its scope. From the above review, the conclusion is inescapable that the progress of the health resorts of this country has failed to keep abreast of the revolutionary advances that have taken place during the last half century in other fields of medicine.

It is to be hoped that the evaluation of spas being conducted by the Council on Physical Medicine and Rehabilitation of the American Medical Association and efforts to place them on a firm scientific basis may alter this discouraging situation, and revive confidence in resort therapy.

The number of old, chronically ill, and disabled people in this country is steadily rising—the result of the national increase in life expectancy. Therefore, it is not only highly desirable, but indeed urgent, that the present professional and popular attitude towards spa treatment should change. To look forward to this is justifiable because the properly conducted health resorts offer the best method of combining the therapeutic advantages of change in climate and environment with a sound health program built around the modern broad concept of physical medicine and rehabilitation.

REFERENCES

1. Sigerist, H. E.: American spas in historical perspective, Bull. Hist. Med. **11:** 133–147, 1942.
2. Sigerist, H. E.: Health resorts, Ciba Symp. 8, no. 1–2 (April–May), 1946.
3. Kornblueh, I. H., and Piersol, G. M.: Mineral springs in the commonwealth of Pennsylvania: a field survey. Arch. Phys. Med. **34:** 566–573, 1953.
4. Kuhn, Adam: Dissertatio Medica Inauguralis, De Lavatione Frigida. Edinburgh, 1767.
5. Rush, Benjamin: Directions for the Use of the Mineral Water and Cold Bath at Harrowgate, Phila., 1786. (Quoted by Shelton (12)).
6. Bell, John: A Treatise on Baths. Phila., 1850.

7. Bell, John: On Baths and Mineral Waters. Phila., 1831.
8. Hinsdale, Guy: Hydrotherapy (with an appendix, "Some truths about hydrotherapy," by Simon Baruch). Phila., 1910.
9. Lockette, H. W.: An Inaugural Dissertation on the Warm Bath. Phila., 1801.
10. The Sunday Bulletin, Phila., 5 Aug., 1951.
11. Green, Doron: History of Bristol Borough. Camden, N. J., 1911.
12. Shelton, F. H.: Springs and spas of old-time Philadelphians, Pa. Mag. Hist. and Biog. **47:** 196–237, 1923.
13. Kornblueh, I. H., Piersol, G. M., and Elias, G. A.: Spas and mineral springs of Philadelphia and vicinity, Phila. Med. **48:** 257, (27 Sept.) 1952.
14. Rush, Benjamin: Experiments and Observations on the Mineral Waters of Philadelphia, Abington and Bristol in the Province of Pennsylvania. Phila., 1773.
15. Hotchkin, S. F.: The York Road, Old and New. Phila., 1892.
16. Bohn, J. Lloyd: Personal communications of partly unpublished data.
17. Jones, Allen: Wellsboro, Pa. Personal communication.
18. Bell, John: The Mineral and Thermal Springs of the United States and Canada. Phila., 1855.
19. Exercises at the dedication of a marker on the site of the old Revolutionary hospital at Chester Springs, 7 Oct. 1916, Bull. Chester Co. Historical Soc.
20. Watson, J. F.: Annals of Philadelphia and Pennsylvania in the Olden Time. Vol. 2, p. 463. Phila., 1868.
21. Futhey, J. S., and Cope, G.: History of Chester County. Phila., 1881.
22. Chester County Historical Society, courtesy, Miss Dorothy B. Lapp.
23. Chester County Historical Society, courtesy, Miss Dorothy B. Lapp.
24. Rischel, C. D.: The Life and Adventures of David Lewis, the Robber and Counterfeiter, the Terror of the Cumberland Valley. Newville, Cumberland Co., Pa., 1890.
25. Klein, H. M. J.: Lancaster County, Pennsylvania. N. Y., Chicago, 1924. P. 217.
26. Ellis, Franklin, and Evans, Samuel: History of Lancaster County, Pennsylvania. Phila., 1883. P. 838.
27. Ellis, Franklin: History of Fayette County. Phila., 1882.
28. Fitch, W. E.: Mineral Waters of the United States and American spas. Phila., 1927.
29. O'Neal, J. W. C.: Contribution to the History and Use of the Katalysine Spring Water, at Gettysburg, Pa., and a Comparison of Its Powers with Waters of Foreign Springs. Gettysburg, Pa., 1876.
30. Coulter, J. S.: Physical Therapy. N. Y., 1932. (Quoted by Wyman in Glasser, O. Medical Physics. Chicago, 1944. (Vol. 1), p. 619.)
31. Africa, J. S.: *ed.* History of Huntingdon and Blair Counties. 1885. (Courtesy, Floyd G. Hoenstein, Publisher, Hollidaysburg, Pa.)
32. Rung, A. M.: Warm Springs: An Ancient Resort with an Unknown Past. (Courtesy, Morley Mays, Dean, Juniata College.)
33. Bushrod, W. J.: American Resorts. Phila., 1889.
34. Walton, G. E.: Mineral Springs of the United States and Canada. 2d ed. N. Y., 1874.
35. Mrs. L. J. Keagle: Canton, Pa. Personal communication.
36. Stearns, N. D., Stearns, H. T., and Waring, G. A.: Thermal Springs in the United States. U. S. Dept. of the Interior. Geological Survey. Water-supply Paper 679-B. Washington, D. C., 1937.
37. Tribune Republican, Meadville, Pa., Meadville Sesqui-centennial Issue, 12 May 1938.
38. Fitch, W. E.: Bedford Springs Co. The Carlsbad of America—the Bedford Springs Resort for Health and Recreation. Bedford Springs, Pa., June, 1928.
39. Bedford Springs Hotel and Baths. Worthwhile Facts for Physicians about the Bedford Mineral Waters. ca. 1930.
40. Disturnell, J.: Springs, Water-falls, Sea-bathing, Resorts, and Mountain Scenery of the United States and Canada. N. Y., 1855.

Memoir of Edwin Grant Conklin (1863-1952)*

By E. B. KRUMBHAAR

PROFESSOR Edwin Grant Conklin†, the first elected member of our new class of Honorary Associate Fellows (1942), was one of the most distinguished biologists in this country and one who had a number of affiliations with Philadelphia science for many years. When I proposed that this College should amend the By-Laws by setting up a new class of non-medical Fellows as a way of broadening its connections with scientific and cultural Philadelphia, Dr. Conklin at once appeared as a most suitable candidate for such a Fellowship.

Of New England-Virginia ancestry, Dr. Conklin was born in Waldo, Ohio, November 24, 1863, entered Ohio Wesleyan University (B.S. 1885), where his interest in science was aroused by close association with Professor E. T. Nelson. Through contacts made late in Dr. Conklin's life, the writer can testify that he retained the familiarity with classical literature acquired in those student days. He held professorial chairs for a few years each at Rust University, Johns Hopkins (where he received his Ph.D. degree in 1891), Ohio Wesleyan, and Northwestern, coming to the University of Pennsylvania as Professor of Zoology in 1896 for a period of 12 years. From 1908 to 1933 he was Professor of Biology at Princeton University; in the latter year he became Emeritus Professor.

In Philadelphia he was promptly elected to the American Philosophical Society where he was shortly put on important committees, was Secretary (1901 to 1908), Vice-President (1932 to 1942), and for six years he also held the newly created position of Executive Officer, was President from 1942 to 1945 and again from 1948 to 1952, and on the Council at the time of his death, November 21, 1952. He was a member of the National Academy of Sciences and President of the American Association for the Advancement of Science (1936). Among other honors, he was an honorary member of six European societies and received eight honorary degrees from American Universities.

Dr. Conklin's life-long interest was in cytology and embryology, progressing through observational, experimental and philosophical approaches. During his Philadelphia period was published one of his greatest works, *The Organization and Cell Lineage of the Ascidian Egg*, based on observations made in the Marine Biological Laboratory at Woods Hole where he spent his summers for 62 years. He also was active in the affairs of the Academy of Natural Sciences (Vice-President 1901–1950), and the Wistar Institute.

Though Dr. Conklin's direct association with our College was neither intimate nor of long duration, he was personally acquainted with many of its Fellows, who could not fail to appreciate his youthful mental vigor, and be glad that we had with us a friend always available for wise and stimulating counsel.

* Prepared and published at the request of the Council of the College of Physicians of Philadelphia.

† The writer is much indebted to Elmer G. Butler's Memoir in the 1952 Year Book of the American Philosophical Society (pp. 5–12), to which the reader is referred for further details.

TRANSACTIONS & STUDIES

of the

College of Physicians of Philadelphia

Volume 21 (Fourth Series)

Number 4 (April 1954)

President's Address*

By RICHARD A. KERN

THIS meeting marks the close of the one hundred sixty-seventh year of this College. In compliance with our law, the agenda call for an Address by the President. Custom has established that it shall take the form of a Report on the State of the College. In addition, this one is a Report on the progress of our campaign for funds to enlarge, improve and implement our facilities. Here there have been some highly important developments that make this year of 1954 a crucial one in the history of the College. Therefore, and above all, this address is a Call to Service directed to our whole Fellowship. Every Fellow, especially each one of the 974 not present at this meeting, should read this message thoughtfully and should dedicate himself accordingly to our cause.

FELLOWSHIP

The Fellowship has again shown an increase during the year. In December, 1952, the total number of Fellows was 959. In December, 1953, their number was 998, of whom 905 were Resident, 2 Associate Resident, 84 Non-Resident, 5 American Honorary and 2 foreign Honorary Fellows.

* Read at the business meeting of the College of Physicians of Philadelphia, 6 January 1954.

Deaths

Death has taken from our ranks during the past year 15 Resident Fellows, 2 Non-Resident Fellows, 1 American Honorary Fellow and 1 Honorary Associate Fellow. As I read their names, the Fellows will please to stand.

Resident Fellows

Francis O. Allen
Herbert B. Carpenter
Henry Dintenfass
William Drayton, Jr.
Henry C. Earnshaw
Robert S. Gamon
Alfred Gordon
Edwin E. Graham
Harold R. Keeler
Louis B. Laplace
Eugene C. Murphy
Charles A. Steiner
Herbert W. Taylor
Louis H. Twyeffort
Charles C. Watt, Jr.

Non-Resident Fellows

Willard H. Kinney
B. B. Vincent Lyon
Robert P. McReynolds

Honorary Fellow

Warfield T. Longcope

Honorary Associate Fellow

William Henry Donner

THE STAFF

I am pleased to report that there have been no deaths and few changes in our Staff. Dr. McDaniel asked to be relieved of his duties as Librarian in order that he might devote himself more fully to historical research, especially in the treasures of our Library. He has accordingly been designated Curator of the Library's Historical Collections, and he will also continue to edit the College publications. In July, 1953, the College was signally honored when Dr. McDaniel was selected to make the opening address to the First International Congress on Medical Librarianship which was held in London, England. Mr. Morse, formerly the Administrative Associate Librarian, has been advanced to the position of Librarian of the College, and he also serves as Secretary of the Hall Committee. Mr. Allen has been made Superintendent of the Building. It is a pleasure to note that under such efficient and devoted stewardship and care, the condition of our building and its contents is at its finest in my experience. Much appreciated are the improved public address systems.

At this point I wish to pay high tribute to our entire Staff for their constant loyalty, smooth efficiency and gracious willingness in the performance of their tasks. Dr. McDaniel, Mr. Morse, Mr. Allen, Mrs. Wade, Miss Lang and every other member of our Staff have each earned our deepest gratitude. I express my particular thanks to Miss Lang whose help I have so frequently invoked, and which she has so cheerfully given.

MEETINGS, SECTIONS AND COMMITTEES

In the same number of the *Transactions* carrying this address will be published the List of the College Lectures presented at our Stated Meetings during the year; also the transactions of the several Sections, and the reports of several of the Standing Committees. It is commendable that the College and the Philadelphia County Medical Society have continued to hold two joint meetings yearly. At some of the Stated Meetings the lecture was supplemented by a panel discussion that added to the interest and effectiveness of the presentation. This device deserves further trial. The programs of the Section Meetings show a high order of excellence. Endowed Lectureships now provide a full quota of speakers for the College Meetings: future benefactors could bring added strength to our Sections by suitable lecture endowments. The reports of our Standing Committees give abundant evidence of the faithful manner in which these committees have served, and they should be read carefully by all Fellows for an insight into the manifold details of the operation of this College.

ALVARENGA PRIZE

The Alvarenga Prize was awarded on July 14, 1953, the 70th Anniversary of the death of the Testator, to Dr. Francis D. Moore, Moseley Professor of Surgery at Harvard University School of Medicine, for his outstanding contributions to our knowledge of the changes in body metabolism following surgical operation. At the November, 1953, Meeting of the College he presented the Alvarenga Prize Lecture, which may be read in the February, 1954, number of the *Transactions*.

MÜTTER MUSEUM

The Mütter Museum continues to attract further valuable accessions. What is more important, its treasures are attracting the largest numbers of visitors in its history, thanks to the fine publicity which the Curator, Mrs. Ella N. Wade, has given our Collection in her articles appearing in *Philadelphia Medicine*. She has now written 43 such articles, 16 of which were published in 1953. They have attracted to the Museum several groups of students from schools and colleges.

PORTRAITS OF PAST PRESIDENTS

There are still six gaps in our collection of portraits of past presidents. It is sincerely hoped that every effort will be made to complete our series. During the year the College received the writer's portrait painted by Mr. Harry Moskowitz of Philadelphia.

THE LIBRARY

The Library has continued to grow in size and usefulness: a few figures are offered in proof. Some 14,000 visitors consulted about 40,000 volumes from the stacks and an unknown number of volumes and journals on the shelves of the reading rooms, and they borrowed nearly 8,400 volumes to take out during 1953. The Library supplied over 3,400 photostats and loaned over 2,600 volumes to 127 libraries in 29 states, the District of Columbia, and Canada. Accessions of books during the year numbered 2,525 and there were received 1,739 journals. A comparison of these with the previous year's figures shows a substantial increase. Our slightly greater income has just managed to support this growth in service.

THE BUDGET

The Budget for the ensuing year, which was adopted this evening, shows how close to the wind we are sailing: With an anticipated income from all sources of $97,565.19, the largest income in our history, we expect to spend $97,546.34, leaving a potential surplus of $18.85. For the second year we have been unable to save anything for unforeseen contingencies, and practically the only additions to our endowment have been the entrance fees of the new Fellows. This is occurring at a time when our over-filled book stacks make new construction imperative.

The Future of the Library

These financial problems and the future of the Library have for several years been the subject of study, planning and fund-raising efforts by the officers and many Fellows. Let me review briefly the outline of those plans and what has been accomplished. *Our ultimate goal* is the raising of $1,500,000, of which $800,000 are for the several aspects of the building program, and $700,000 are for endowment. In January, 1952, Dr. Miller reported the tentative promise by a certain foundation outside of this city to give us $250,000, if we first raised $1,250,000. In January, 1953, I could report that through the good offices of Dr. Miller, the Donner Foundation had promised us $100,000, if we first raised $1,500,000. This was, and still is, our long-range objective; an objective that seemed almost beyond our hope of achievement. (Moreover, the tentative gifts of $350,000 by these two foundations would be for endowment, and not for building purposes.) Nevertheless, we have worked hard to this end, and by November last had received from Fellows and their friends about $125,000 in cash. This included a splendid gift of $10,000 obtained from Smith, Kline and French Company, largely through the good offices of Dr. Miller.

Then, two months ago, a Friend of the College, who insists on remaining anonymous, made us the promise of $100,000 for construction purposes, provided that we first raise a total of $400,000 by 31 December 1954, and provided further that we begin construction in January, 1955.

Here is a new and immediate goal, a goal that is certainly within our power to reach, and which, if reached, will solve the problem of our greatest need (stack space and a modernized heating plant) within a year. I announced this objective for 1954 in a special letter on 18 December to all the Fellows, urging them to make every possible effort to raise the $269,000 needed. The response has been very encouraging, with additional gifts coming in since mid-December totalling over $17,000. These include a gift of stock worth $6,134 at current market value, obtained from Mr. Harold H. Kynett by Dr. Joseph VanderVeer, and a gift of $1,000 from the Section on Ophthalmology. *As of today, we must raise $252,000 by 31 December 1954.* How can we do it?

1. *First of all, the Fellows must give.* There are 447 Fellows who to date have given nothing: at least 90 per cent of these can and should give. What is more, I am confident they will, for there have been 28 new givers among the Fellows within a month. Those Fellows who have given should give more, if they pos-

sibly can. Here, too, the record is even more encouraging, for a larger number have given additional gifts within a month.

2. *More important, the Fellows must get gifts from their friends and patients.* Here the picture is encouraging in what those who tried have accomplished, and disheartening when one notes the small percentage of the total Fellowship that made any effort to obtain gifts. Fellows have a way of dodging this issue by saying, "I am a *poor* beggar". Yet the record shows that the 76 Fellows, who did try, got $48,314, or $635 per Fellow. But over 900 Fellows have made no effort: they are *unwilling*, not *poor* beggars.

I fear that many of us are also *lazy* beggars. At least, I am sure that every Fellow could secure many fine gifts by simply writing some letters in *long-hand* to potential donors. To prove this point, I furnished every Fellow in mid-December with a copy of a letter which he was urged to send to some prospects. Between the 18th and the 21st of December I sent that same letter, written by me in long-hand, to 91 persons. As of today, I have received in reply to those 91 letters 34 contributions totalling $4,245, and in each instance sent with the thanks of the donor for the opportunity for service. During this same period just 16 other Fellows have obtained contributions. This month I shall again send to all Fellows a copy of that letter, together with the score of what it produced for me, in the hope that they will make an all-out effort along these lines. The question has been asked: is there any limitation as to the prospects to whom Fellows may appeal? The answer is: they may appeal to any individuals. They may also approach any groups of firms outside of Philadelphia. But please leave all the foundations and the firms in Philadelphia to your officers. But give us suggestions about these, if you can.

I would be remiss if I did not thank the Fellows for what they have already done in this Campaign. By personal gifts or solicited funds or both, 18 Fellows each have raised between $500 and $1,000; 31 have raised between $1,000 and $2,000; 1 has obtained nearly $7,000, 1 has secured nearly $9,000 and 1 a little over $9,000. The example set by these 52 Fellows should be an inspiration to us all.

3. *Your officers are continuing their efforts with firms and foundations.* We are sure to receive some substantial gifts from these sources in the near future.

But let us also remember the long-range goal: we must increase our endowment to meet the growing budgets of future years. To be sure, the entrance fees of new Fellows accrue to this purpose, and in the five years of our campaign they have added $12,450 to our funds. You should therefore be alert to your duty to propose worthy candidates. The James Harold Austin Memorial Fund, which has now passed the $1,500 mark, is another step in this direction. It, too, is deserving of your further generosity.

Legacies, however, have been the chief source of our approximately $800,000 in income-producing assets. These legacies have come to us over the years from many sources, the great majority from Fellows. It is therefore the more disturbing that in the last 5 years, during which 69 Fellows died, only one mentioned the College in his will, and his bequest will not be available to us during the survival of his residuary legatee.

What about *your* will? Surely, most of you could make provision for some bequest to the College without detriment to your family. Here is your finest opportunity to create a lasting memorial that will continue to serve your College in the years to come. Several of you have written me that you have already made such provision. I urge you all to write such a codicil as soon as possible, and please do not restrict its usefulness too closely, but set it up in general terms, such as, "the income to be used for the purposes of the College, as its Council shall direct", or "the income to accrue to principal, and income and principal to be used in future major building programs of the Col-

lege, as its Council shall direct". In that way you can help the Building Fund Drive of a future generation of Fellows. *Please do this now.*

This year of 1954 is indeed a crucial one in the history of the College, for in this year either we will put across the first big project to which we have set our hand in nearly half a century, or by our failure we will let our magnificent library slip from its high estate into third-rate mediocrity. Before 359 days have passed, we must raise $252,000: that means an average of $700 on every single day. Here is our challenge. I hope and pray that each of you will rise to the occasion.

Annual Report on the Library*

ADMINISTRATIVE

The Journal-Selection Policy

The expository section of this year's annual report undertakes a restatement of the library's long-standing journal-selection policy. The validity of this policy is examined in the light of two sets of library records and the origins of the policy are considered in terms of factors peculiar to this library as well as the more universally applicable criteria. Particular attention is paid to the principle of regional cooperation.

The Policy

It must be admitted that the policy has evolved in part through a process of restricted coverage in certain fields. This de-emphasis has been made possible because of the existence of outstanding libraries in the following subject fields in the city: general science, the natural sciences, chemistry, dentistry, veterinary medicine, and pharmacy. Journals written solely in the Oriental or Slavic languages have not been collected because of the small demand for such materials and the availability of photocopies from the Armed Forces Medical Library, which has better developed avenues of acquisition for these journals. Society journals which serve primarily as local news organs are kept only for Pennsylvania and the Philadelphia metropolitan area.

After these blocks of minimal coverage are determined, the library attempts to acquire as many of the journals indexed in the *Current List of Medical Literature* and the *Quarterly Cumulative Index Medicus*, and abstracted in the *Journal of the American Medical Association* and other media, as its budget will permit. When the library is considering new subscriptions it watches the traditional indications of quality such as: prestige of the sponsoring society, reputation of the editors and contributors, presentation of hitherto unrecorded case material or laboratory research, bibliographical support of data, quality of photographic reproduction, and coverage by indexes and abstracts.

The two sets of records which serve as the springboard for this study are (1) a four year and nine months' study of this library's journal "nots" and (2) a sampling of the library's recent journal circulation.

The Hads and The Had Nots

"Nots"

Special attention to "nots" has long been one of the keystones of circulation desk routine. The library's patrons write their own call slips and are encouraged to submit these requests without checking the journal catalog to determine whether the volume is in the library. If the volume requested is not located, a member of the staff checks the catalog. When this procedure shows an incomplete volume or missing volumes, the reader's slip is marked "not page" or "not volume" as the case may be. When the requested title does not appear in the journal catalog, it is always verified in one of the periodical guides such as: The Union List of Serials, The World List of Scientific Periodicals, World Medical Periodicals, or the lists of journals covered by the *Current List of Medical Literature*, the *Quarterly Cumulative Index Medicus*, *Biological Abstracts*, or *Chemical Abstracts*. After the title is verified, the reader is told that the library lacks the title. The call slip is then marked "not" and whenever possible the reader is given the name of another library which receives the title. If the title is not verified, the reader is asked for his complete reference and the source of his citation. Such a routine check recently showed that a printed reference to the *Journal of Biology and Medicine* had lost the all important initial *Yale*.

* 1 November 1952–31 October 1953.

So What "Not"

The tabulation of almost five years of "misses" was undertaken to determine whether or not they tell a story rather than to fortify any preconceived theory. It is unlikely that the inventory of "nots" really proves anything, but for those who are concerned with the inner workings of this particular library, they may add perspective and stimulate conjecture.

3,012 to 237,257. During the four year nine month period under study, 3,012 requests for journals were not filled because the library did not own the reference at the time of the request. During this same brief period, the library had a total journal and book circulation of 237,257†. Percentage-wise the "nots" under observation constitute only 1.26% of the library's circulation. This might then be considered a study in library microbibliography.

Out of Scope

A close examination of the 3,012 "nots" shows only 1,990 within the scope of the library as given in the statement of policy above. If this legerdemain is permitted, the "missed" average would be reduced to .827%. The leading "out of scope" categories were: chemistry, 252; general science, 212; pharmacy, 139; veterinary medicine, 85; dentistry, 83; zoology, 73; mathematics, physics, and statistics, 34; botany, 34; agricultural sciences, 24; and all others, 114.

When "Not"

In order to determine any chronological pattern of unfilled requests, the "nots" were tabulated by decades as follows:

1900's—	74
1910's—	69
1920's—	213
1930's—	592
1940's—	1,386

† Separate figures for journal and book circulation are not available for all of this period. Statistics for 1952 and 1953 show a nearly four to one ratio of journals to books.

The period from 1950 to 1953 accounted for 521, which in consideration of the shorter period involved, would seem to be the period of heaviest demand. Unfilled nineteenth century requests amounted to 126. There was one eighteenth century reference which was not supplied and 29 "nots" had no date. This would seem to show that efforts to fill gaps could concentrate on the last ten years. The 1952/53 report of the Yale Medical Library finds that "the 'current use' of a journal appears to continue for about five years, with the second year after publication being the time of heaviest use."

We suspect that the high incidence of "nots" in the 1940's may have been caused in large part by delayed wartime issues which have since been acquired.

Which "Nots"

Before returning the "not" file to the limbo of storage boxes, a list was made of all the titles represented by five or more requests. There were 116 such titles in a total of 1,401 titles. While it is sobering to find 1,401 different titles appearing in 3,012 requests, it is comforting to realize that only 95 of the 116 titles are given in World Medical Periodicals, which indicates that this segment of the material would be largely within the scope of most general medical libraries. However, the unwritten policy of Philadelphia regional cooperation justifies, in our opinion, a more limited scope for the College of Physicians. Nevertheless, it is gratifying to be able to report that the library is now regularly receiving 64 of the 116 titles, some of which are no longer being published. While it would be inaccurate to ascribe these subscriptions to users' requests alone, the value of our readers as journal-selection advisory board is genuinely appreciated.

Ten "Nots"

The ten "nots" most frequently called for, in order of their demand were: *Helvetica Chimica Acta*, *British Dental Journal*, *Journal of Experimental Zoology*, *Canadian Journal of Research* (all sections), *Physiological Zoology*,

Berichte der deutschen chemischen Gesellschaft, *Bollettino della Società Italiana di Biologia Sperimentale*, *Archiv der Pharmazie*, *Journal of the Chemical Society of London*, and *Journal of General Psychology*. Although only three of these are within this library's conception of its scope, compromise to reader demand has been made by subscribing to six of the titles.

In order to make the story complete, each title would have to be studied individually. For example, all of the *Journal of Experimental Zoology* "nots" were for volumes prior to 1940; the library now receives this title regularly and has completed its file back to 1934. The library has subscribed to *Bollettino della Società Italiana di Biologia Sperimentale* since 1948 and enjoyed an exchange agreement through 1939. All but one of the "nots" were between 1941 and 1947. The unfilled requests for *Journal of General Psychology* were all prior to 1944.

The small percentage of "nots" seems to indicate that the library's journal-selection policy is reasonably sound.

Sample of Current Circulation

The second tabulation is intended to show what this library's customers were actually requesting and receiving during the most recent twelve month period. The tabulation was made from two consecutive runs of slips selected at random from the year's circulation. A total of 6,086 circulations was tabulated from a twelve months' circulation of 30,953 journals. As in the case of the "nots", these figures may only be indicative of the demand of the clientele of this particular library. Certainly, the unique position of the library in its community would make generalizations hazardous.

More than 900 different titles were supplied in the 6,086 circulations tabulated. This great diversity of requests would complicate any attempt to supply less than the total lists of periodicals indexed in the *Current List of Medical Literature* and the *Quarterly Cumulative Index Medicus* unless a consistent criterion of selection were established.

Practical Applications

This tabulation has produced a list of the most-requested journals which will enable this library to re-examine the list of journals which, for convenience, are shelved at present in the reading room. Some of these titles may no longer be in sufficient demand to justify their favored location. The list of titles in greatest demand will also show which duplicates the library should keep to build a reserve file which could be called upon when the first copy is in circulation.

In anticipation of the day when a new stack area will force the library to decide which volumes to move into less convenient locations, a tabulation of two date periods has been made. This inventory shows that from the total sample of 6,086 circulations, 264 were in the period before 1900 and 407 were in the period, 1900–1924. This would seem to demonstrate the feasibility of a separate stack area for journals of the nineteenth century and earlier.

The 50 most requested titles, in the order of their popularity, were:

Journal of the American Medical Association
Journal of Biological Chemistry
American Journal of Physiology
Proceedings of the Society for Experimental Biology and Medicine
Lancet
Journal of Clinical Investigation
British Medical Journal
Annals of Surgery
Biochemical Journal
American Journal of the Medical Sciences
Surgery, Gynecology and Obstetrics
American Journal of Obstetrics and Gynecology
Journal of Bacteriology
Nature
New England Journal of Medicine
Annals of Internal Medicine
Journal of Laboratory and Clinical Medicine
American Heart Journal
Science
Comptes rendus des séances de la Société de Biologie
A. M. A. Archives of Pathology
A. M. A. Archives of Internal Medicine
Journal of Physiology
American Journal of Surgery
Circulation

A. M. A. American Journal of Diseases of Children
Surgery
New York State Journal of Medicine
Cancer Research
American Journal of Ophthalmology
Journal of Experimental Medicine
Journal of Pediatrics
A. M. A. Archives of Ophthalmology
Annals of the New York Academy of Sciences
Surgical Clinics of North America
Proceedings of the Royal Society of Medicine
A. M. A. Archives of Surgery
American Journal of Clinical Pathology
American Journal of Psychiatry
A. M. A. Archives of Neurology and Psychiatry
Journal of Thoracic Surgery
Psychoanalytic Quarterly
American Journal of Medicine
Presse Médicale
Deutsche medizinische Wochenschrift
Biological Abstracts
Virchows Archiv für pathologische Anatomie und Physiologie
Journal of Pharmacology and Experimental Therapeutics
Journal of Clinical Endocrinology
American Journal of Roentgenology

The Policy Amplified

With the tabulation of our data behind us, we wish to amplify the brief statement of scope and policy made at the beginning of this report. We propose to do this by (1) describing the position of the library in the local community; (2) indicating the nature of the library's present collections and subscription lists; (3) evaluating the needs of its readers as revealed by their requests; (4) comparing the library's current journals with lists of indexed and abstracted journals.

(*1*) *The Philadelphia Story*

Philadelphia's library heritage from colonial days is a number of fine society libraries which have collected in certain fairly well-defined fields. This inherited cooperation was detailed in a survey published in 1942 in "Philadelphia Libraries, a Survey of Facilities, Needs and Opportunities, a Report to the Carnegie Corporation of New York by the Bibliographical Planning Committee of Philadelphia".

The 1942 survey characterized the Library of the College of Physicians as "one of the finest medical libraries in the world", while describing the Library of the Academy of Natural Sciences as "outstanding among the libraries of natural science in America" and the Franklin Institute Library as "notably strong in the physical sciences, in chemistry, and in electrical engineering". The same survey provides this library's justification for not attempting fuller coverage of the field of dentistry when it says, "the library at the University of Pennsylvania School of Dentistry (The Evans Institute) . . . is probably the finest dental library in the world." The existence of a specialized library at the University of Pennsylvania for its School of Veterinary Medicine has relieved us of primary responsibility in that field. The need for more than a minimal collection in pharmacy is obviated by such strong libraries as the Philadelphia College of Pharmacy, Temple University, and the pharmaceutical libraries of Sharp & Dohme, and Smith, Kline, and French. Buttressed by these fine collections in the collateral sciences, the College of Physicians has been able to stick more closely to its knitting than would otherwise have been the case. Philadelphia's medical school collections have a greater influence on this library's book-selection policy than upon the journal-selection policy which is under study in this report.

As important as the library's relationship to other Philadelphia libraries is its relationship to its clientele. Most of the library's users have easier access to another library which might be considered their primary library. It might be logical to suppose that these people would have exhausted the resources of their own libraries before visiting a library more remote from their classrooms and laboratories. Many of the Fellows of the College themselves serve on the faculties of the medical schools or have access to hospital libraries. The second recourse function is also performed through a lively inter-library loan service to the local libraries. For these reasons, the College feels

justified in not duplicating many of the journals in the allied sciences which are easily obtainable elsewhere, preferring to buy some of the strictly medical material which would not otherwise be available in the city. This is an application of the economic principle, common to business enterprise and household finance, that you cannot spend the same dollar twice.

(*2*) *The Basic Collections*

The library's journal-selection policy is consciously conditioned in part by the library's traditional strength in certain subject fields. Gifts of libraries and endowments have encouraged emphases in dermatology, ophthalmology, radiology, gynecology, obstetrics, pediatrics, and surgery.

(*3*) *Demand*

The list of the 50 most requested titles contained in this report seems to be a contradiction of the position of this library as a secondary one for most of its readers. Most of the titles in the first 50 would certainly be in all medical libraries. We are forced to conclude therefore that many readers do use this library first. Although the diversity of its holdings may actually attract the readers, their use of the basic indexes leads them to call for the standard journals in about the same preponderance as would be expected in a smaller library. The large number (over 900) of different titles requested in our sampling confirms the first suspicion, however, that readers are taking advantage of its extensive journal holdings.

The library's interest in the needs of its users is well enough known to encourage reader recommendations. The library's preservation of a "not" file is further demonstration of this interest. An attitude of compromise with its readers' demands has led the library to maintain complete files of many journals which would otherwise have been considered "out of scope".

(*4*) *Indexed Journals*

The presence of a new journal in the familiar indexes is soon felt by the library. In an effort to anticipate this demand, the library faithfully checks all such lists of periodicals indexed and abstracted with a view to obtaining as large a degree of completeness as budgetary considerations and free mailing lists will permit. A few examples of such checking follow.

In September of 1950, the library checked the first three issues of the newly re-designed *Current List of Medical Literature*. At that time it was receiving or had on order 914 of the titles indexed while 353 were not being received. However, only 53 of the missing titles were in English and 27 of the 53 were in subject fields not generally covered by the library. It was also noted that 102 of the titles were in Slavic tongues. Nevertheless, this examination of the lists of indexed journals resulted in additions to the library's files.

More recently, in November 1953, the library checked the list of 154 journal titles which are regularly analyzed in *Annales de Dermatologie et de Syphiligraphie*. There were only 17 titles which were not being received regularly. As a result of this check, six new subscriptions were entered with the library's agents and two begging letters were dispatched to journals which were thought to maintain free mailing lists. Special funds left to the library by Dr. Louis A. Duhring for literature in dermatology put the library in a favored position in this instance.

The December 26, 1953 issue of the *Journal of the American Medical Association* listed 292 titles as being abstracted in the Current Medical Literature Department. All but four of these titles were being received regularly and the library has taken steps to complete its coverage of this list.

ACKNOWLEDGEMENT

This evaluation of the library's journal-selection policy brings to mind the many people who have contributed to the building of the library's journal files and subscription lists. The continuing support of this library through the 167 years of its existence by the Fellows of the College has put it in a position to be able to offer a respectable portion of the world's

medical literature to its present generation user. Credit must be given to present library staff members and their predecessors through the years whose good judgement is reflected in the library's low "not" average. For the counsel which made this judgement possible, thanks must be given to generations of library committees and other informed users of the library who shared their subject knowledge so generously. The original planners and contemporary builders of medicine's indexes and abstracting tools have charted a path through the literature and their selections have been copied unashamedly. Special gratitude is owed to our professional colleagues who have shared the results of many years' professional experience in the literature of librarianship. The value of the "Handbook of Medical Library Practice," the interchange of annual reports, and the articles in the *Bulletin of the Medical Library Association* cannot be underestimated. In this area, the idea of regional cooperation would have remained theoretical if it had not been for the Philadelphia Union Library Catalogue. As individual journal titles are added or dropped we contribute to the pattern much as the mosaic tile setter in a cathedral. The pattern is not wholly ours and there is much work to be done.

The College Library in 1952–1953

Personnel

To maintain the continuity of the library's own history, as reported in these pages, record is made of the appointment of the former Administrative Associate Librarian, Mr. Elliott H. Morse, as Librarian of the College, effective June 1, 1953. Mr. W. B. McDaniel, 2d, the former Librarian, as Curator of the Library's Historical Collections, will devote his entire time (aside from editing the College's *Transactions & Studies*) to developing the historical aspects of the library's services. The library's recognized wealth of historical materials, and its previous inability to utilize them fully, makes this a most significant development in the library's own history. The potential benefits to the library are particularly enhanced by Mr. McDaniel's long association with and intimate knowledge of the library's historical materials. The administration's aspirations for a complete Rare Book and Medical History Department are previewed by the curator in the historical section of this report.

The new Librarian records here his great gratitude to the former Librarian and the members of the library staff for their patient and sympathetic tutelage during the period of his apprenticeship.

The other administrative changes noted in the staff roster at the end of this report took place after the close of the current report year and will have to await next year's report for fuller exposition.

Medical Literature Service

The library administration has long suspected a need for special assistance to its clientele which is clearly beyond the available time of the regular staff. After a questionnaire established this need, the library committee authorized the establishment of a Medical Literature Service on October 1, 1953. Prior to the organization of this service, the Librarian studied similar services being offered by the New York Academy of Medicine, the John Crerar Library, and the American College of Surgeons. The generous cooperation of these libraries made a confident beginning possible in this library. The library secured the services of Mrs. Virginia Beatty as Director of the Service. Mrs. Beatty majored in science at Purdue and received her library degree from Columbia University. She was awarded a scholarship by the Medical Library Association for additional studies in medical librarianship.

The Medical Literature Service offers translating, abstracting, and other bibliographical services such as the compiling or checking of lists of references. The Service will also supply a periodic listing of current literature on specified subjects. The rates for these services are available upon request. The initial response to this Service has been reassuring and the ad-

ministration believes that a real need is being met effectively.

Professional Staff Activity

Mrs. Elizabeth Bready has been appointed chairman of the Medical Library Association's Committee on Periodicals and Serial Publications. In this capacity, she is editing *Vital Notes on Medical Periodicals.* This record of births and deaths in the medical journal world has been welcomed joyously by medical bibliographers who have long despaired over the vagaries of the medical journal.

The Philadelphia Regional Group of the Medical Library Association has appointed the following staff members to its committees: Mrs. Miragliotta to the Membership Committee, and Mr. Morse to its Program Committee. Miss Muriel Hodge served as moderator of the group's symposium on reference tools in the biological sciences. Mr. Morse was chairman of the group during its 1952–1953 season.

The Special Libraries Council of Philadelphia is being served by Miss Muriel Hodge as a member of its program committee, by Mr. William K. Beatty as chairman of its employment committee, and by Mr. Morse as managing editor of its *Bulletin.*

Mr. McDaniel was elected to Honorary Fellowship in the Cleveland Medical Library Association in recognition of his contribution to the survey of the Association undertaken last year.

Mr. Morse represented the library at the annual meeting of the Medical Library Association held in Salt Lake City and accepted an appointment to the association's program committee.

Benefactors

A list of the donors of books and other library materials appears in the statistical section of this report.

The library is pleased to be able to record the following subscriptions to the support of the library made under the terms of the Contribution Plan. The first four companies on this list have supplemented the required subscription with an additional donation.

Sharp & Dohme	$1,000
Smith, Kline & French	1,000
Wyeth Laboratories	1,000
McNeil Laboratories, Inc.	100
National Drug Company	500
Air-Shields Inc.	30
J. T. Baker Chemical Co.	30
Dorfman & Pechner	30
E. I. duPont de Nemours Experimental Station	30
Gray & Rogers	30
Hercules Powder Company	30
La Wall & Harrisson	30
MacAndrews & Forbes Company	30
Quaker Chemical Products Corp.	30
Lee Ramsdell & Co., Inc.	30
Richter Lord & Farage	30
Rohm & Haas Company	30
Samson Laboratories	30
Vale Chemical Co.	30
Henry K. Wampole & Company, Inc.	30

E. H. M.

HISTORICAL

A movement begun some six or seven years ago, and followed more or less desultorily year by year in these reports, results now in, in addition to more important administrative changes, the creation of the post of Curator of the Library's Historical Collections. One does not ordinarily turn to a five-months-old babe for a lucid account of his origin or a philosophical disquisition on the charms and perils of the new situation in which he finds himself. But supposedly there are exceptions, and the new Librarian of the College has graciously interpreted this as one of them.

It is well known to the Fellows, as to many others at home and abroad, that the library contains very superior collections of original and secondary material fundamentally associated with the long and complex history of the medical sciences. Mere pride of possession, whether of individual or institutional character, is no longer a widely respected attitude, of course; a deepened sense of moral values now inclines us to think rather in terms of enlightened trusteeship of the public interest. And it is clearly those terms which have guided

the Fellows in their large development of the library's services in recent decades.

In this development, unfortunately, the historical area failed of that loving care that might have kept its development in step with other developments. This was not by intent (indeed, it ran violently counter to it), nor by accident, but the result of too limited skill at mathematics and in human engineering; the responsibility was never overlooked, its proper assumption merely, and of necessity, put on ice. The embryonic Curator now hopes in some small measure to aid in the extension of the principles of enlightened trusteeship to this neglected area.

Some Aspects of the Basic Problem

Though the fame of our historical collections is widespread, the ironical fact is that the library is itself not able to support the collections' admirers with the analytical statistics and evaluations expected to be available for such research treasures. We know that, as of the terminal date of this report, we have 417 incunabula and 787 manuscripts. We know that 20 years ago there were said to be approximately 14,000 volumes in the great Samuel Lewis collection of *rariora*—now largely merged in the general library; and that there are roughly 4,000 volumes in the notable Samuel D. Gross Library. The records show holdings of some 57,000 theses (starting from the 17th century) and some 231,000 pamphlets —many thousands of them uncatalogued and many thousands of which would, in our experience, be found to be of great rarity and research value. We know that there has never been a year in the past twenty years that has not seen extensive and important additions of all types to the historical collections. Two large and important libraries (Packard and Krumbhaar), received in recent years, we know are still awaiting processing.

Against the obvious fact of these rich accumulations of 167 years has to be placed the less obvious, but nonetheless ineluctable, fact that this material has never been adequately organized for use. There are two quite understandable reasons for this: 1) the annual increment of all types of material year after year far exceeded the time available for adequate processing; where time was lacking, the historical (this being also a "working" library) was inevitably sacrificed to the contemporary; 2) the larger part of the historical material was acquired before there was general recognition of the fact that the cataloguing requirements of historical scholarship and bibliography involve not only specialized knowledge and techniques but even—at the risk of sounding metaphysical—a type of *thinking* often alien to other disciplines. A violinist and a flutist, for instance, may use the same type of music stand, observe many of the laws of music in common; but when they lift up their instruments to play, they begin to use different sets of not only physical, but also mental, muscles—and neither conductor nor audience expects them to be equally competent on both instruments, though theoretically there is no reason why they could not be.

Want of cataloguing, and deficient cataloguing, argue, of course, want and deficiency in respect of the special indexes that really put such material to work—a state rendered even more serious by the fact that this material is largely stacked, in medical subject classes, in the general stacks, with the result that recently acquired rarities of the 16th to 18th centuries will be found rubbing shoulders with the latest lucubrations on the same subjects emanating from today's presses. Under these conditions, there is almost incredible physical maltreatment of precious research material, inadequate knowledge of its content, and almost total inability to obtain the perspective on it needed for intelligent evaluation of its strengths and weaknesses. We have indexes of sorts to portraits (but not to other, equally useful, types of illustration); to printers and illustrators; autograph inscriptions; bookplates—all essential to such a collection. But, alas, how tremulously we use them a recent incident will show. A visiting Britisher doubted that we had a

portrait of him. We turned to the index; there he was. With a smile, he asked if the journal could be brought down. The portrait was that of the subject of his article: it had no legend, but our visiting author's name had been used as the running head of the page on which the portrait appeared. Indexes, we know, are only valuable in proportion to their accuracy; without accuracy, they can create only mischief.

The ultimate goal of a properly equipped and staffed Historical Room waits on a successful culmination of the current campaign for building and endowment funds. Meanwhile, it has been estimated that a grant of $8,000 a year for three years, plus $5,000 for working equipment, would enable us to start at once to provide a catalogue and indexes suitable for historical and bibliographical use and more faithfully representative of the collections' capacity for service.

Carpe diem

Though the present is a transient article, it is yet a recognizable entity, with conditions peculiarly its own. It well may be asked in what ways, under these formidable circumstances, a Curator of Historical Collections may serve the library and its users while the fire is still boiling under the pot that is cooking the future.

Perhaps the most fundamental immediate opportunity is that of fermenting a mental climate in which *thinking* "Historical" (to revert for the moment to the metaphysical) may become in time an automatic process in the calculations of readers and staff alike. This is understandably a matter of slow growth when the operating group is relatively small and long accustomed to not very specifically defined areas of personal responsibility; when there are no obvious physical changes to dramatize the event; and when new concepts perhaps deny in some measure the exercise of old habits of thought and action. Hypothetically, for instance, a curator of historical collections not installed in semi-independent quarters and being used to wider responsibilities on the same scene might easily forget now and then, or even consciously violate, the limits of his present franchise. In turn, only token support might be forthcoming for one reason or another from "circulation and reference" or from the library administration; "periodicals" might be inattentive to its capacity for assistance; "cataloguing" might find anything but a minimum use of, or a minimum contribution to, "historical" an encouragement of encroachment on what it regarded as its province; and so on. In short, a large part of "Historical" 's immediate, direct use to users, in the present and forever, must be engineered by the staff itself, as we gradually learn to *think* "Historical", and thus to encourage users of the library to do the same. Growth processes demand, among other things, time, patiently administered.

Recent directives of the Librarian will help to clarify for the Fellows the present status of a fluid process. The Reading Room reference service will continue to apply itself to any questions that can be answered from the fairly extensive reference sources in that room; or from a book or two brought down from the stacks. In the nature of things, there will be many small questions of historical fact, or that perhaps involve instruction in the use of the catalogue or reference sources in the room, that can be most expeditiously handled there, at their source. To the Curator are referred historical problems requiring more time and freedom of movement than would be expected to be available to the busy Reading Room librarian, and that would, in other respects, normally be thought to fall within the province of a curator of historical collections.

The Curator is to hold himself available for consultation regarding the cataloguing of historical material, but has no further responsibility in that field. "Cataloguing" supplies him with a copy of the main entry card for each historical work catalogued, both for current use and as a start toward development of the separate historical catalogue that will be required when the historical service has its own quarters. With this card and the book in hand, he may then provide himself with such further cataloguing and indexing as he believes to be potentially useful.

A generous sum is allocated to the Curator for the purchase of rare books and other historical material; selections for purchase within this sum, and recommendations for further purchase, are his responsibility. He, of course, prepares all the historical exhibits, reports regularly to the Library Committee and the Council on accessions and other activities, and serves as liaison officer between the library and extra-mural historical endeavors. Not forgotten in all these calculations is the expectation that, given some leisure, the Curator shall himself make use of the collections for research and publication.

Among the earliest special projects to be undertaken is, of course, the gradual extraction and separate shelving of the now submerged books of the 16th to 18th centuries.

In sum, while aspirations and most activities focus on the ultimate goal of a History of Medicine division in the library, adequately organized, housed, and staffed, the day by day motto is *Carpe diem; quam minime credula postero*—Take hold of today, relying as little as possible on the morrow. It is our hope that historically oriented users of the library may become more and more aware of the fact that there is already in residence, in a room entered from the southwest corner of the Periodicals Room, a Curator of Historical Collections specifically charged with the duty of rendering them every possible assistance in the use of those collections. A Curate, moreover, with an abiding desire to help make these treasures better known and more useful to the library's present and future parishioners.

Accessions in the Past Year

Very good. Because of the length of this report, more detailed comment on the historical accessions is reserved for a later occasion. For the present it must suffice merely to note the continued important donations from the library's incomparable friend Dr. Krumbhaar, and the steady interest and support of Dr. Thorington, Dr. Chance, Dr. Bradley, Dr. Radbill, Dr. Leaman, and numerous others of the officers and Fellows.

Exhibits

The 500th anniversary of the birth of Leonardo da Vinci was commemorated by a major exhibit. In preparing for it, we were disheartened to find that, though it has the 6-volume *Quaderni d'anatomia*, published in Christiania, 1911–16, the library did not have the complementary Sabachnikoff and Piumati *Dell' anatomia*, Fogli A and B, 1898, 1901. Too late for this exhibit, incidentally, but no less warmly welcomed on that account, was the copy of Fogli B that turned up among Dr. Krumbhaar's late-1953 donations.

The second major exhibit was devoted to the library's William Harvey Collection—one of the most notable in existence and, to the best of our knowledge, exhibited then for the first time in its entirety.

As usual, the meetings of the Section on Medical History, and the six lectures in its course for students, were provided with appropriate smaller exhibits.

As the major exhibits call for the selection and annotation of 60 to 70 items, the time demanded for their preparation is not inconsiderable. It is hoped that time may now be found for the preparation of four major exhibits a year, the maximum that would seem to be economic when preparation-time and the leisurely rate of potential visitor saturation are balanced.

Other Activities

The Curator attended and, by invitation, addressed the first International Congress on Medical Librarianship, held in London, in July. His traveling expenses were very graciously and generously met by a number of members of the Council of the College, acting in concert with the Section on Medical History. He attended also a two-day meeting of the Medical Library Association's Committee on Bibliography, held in New York. He continued to edit the College's *Transactions & Studies*. A number of book-reviews appeared over his name or initials.

W. B. McD., 2D

STATISTICAL SUMMARY

Inventory

	1953	1952
Total number of accessioned[1] items	183,991	181,473
	1953	*1952*
Incunabula	417	416
Manuscripts (including a few typescripts)	787	785
General	178,610	176,185
Accessioned pamphlets	4,177	4,087
	183,991	181,473
Total number of unaccessioned[1] items	324,312	323,492
Reports	27,568	27,065
Periodicals "reserve"[2]	9,002	8,932
Theses and Dissertations	56,832	56,667
Pamphlets and reprints	230,910	230,828
	324,312	323,492
Total number of current periodical publications regularly received	1,739	1,710
Portraits[3]	85,836	81,441

Distribution of This Material

	Accessioned Items	*Unaccessioned Items*
General Library (including the Lewis Library)	179,644	324,308
On permanent deposit:		
Gross Library	3,930	4
Parry Library of the Obstetrical Society of Philadelphia	217	0
Mütter Museum[4]	200	0
	183,991	324,312

Current Periodicals

	Purchased	*Exchange or Gratis*	*Total*
U. S. A.	320	347	667
Western European Continent	603	57	660
Latin America and West Indies	37	104	141
United Kingdom and Eire	116	31	147
Canada	6	26	32
Eastern European Continent	4	4	8
Asia	25	30	55

[1] Accessioned items in this library comprise the total number of bound volumes and such unbound pamphlets as have been catalogued as separate bibliographical units regardless of their size.

There remain many thousands of unaccessioned pamphlets awaiting accessioning and cataloguing. A true quantitative and qualitative picture of the library's holdings can not be presented until this wealth of neglected material has been processed and duly registered in our 'accessioned', or 'volume', count.

[2] More-or-less complete duplicate volumes of periodicals.

[3] Including 122 oil, and 425 other, framed portraits in the care of the Committee on College Collections. The count of portraits represents the number of entries on the cards in the portrait catalogue. The entries represent, in turn, both loose portraits and those in books, many of them, of course, being merely different reproductions of a single original.

[4] The books of the Mütter Museum are not permitted to be removed from the College building.

Africa	4	6	10
Pacific	4	15	19
Grand Total: 1953	1,119	620	1,739
Grand Total: 1952	1,069	641	1,710

New Titles: A total of 67 periodicals was added in 1952–53. Forty-six of these were purchased; twenty-one received in exchange or gratis. Forty-five began with volume 1.

Separate Issues received, checked-in on the cards, and shelved totaled 13,838. In addition, thousands of duplicate issues were received, as usual; 70 of these were retained for our 'reserve' files, no attempt being made to count those held merely for exchange or other use.

Visitors to the Norris Room for the year totaled 4,698.

Readers' Use of the Library

Library Hours. The library was open, during the academic year, from 9:30 to 9:30 on Mondays and Wednesdays; from 9:30 to 5:30 on the other weekdays. During the latter half of June, in July, August, and the first half of September the library was open from 1 to 9:30 on Tuesdays; from 9 to 5 on the other weekdays, except Saturdays, when it was closed. The following legal holidays were observed: Thanksgiving (beginning at 5:30 on the preceding evening), Christmas and New Year's (and the half day preceding each), Memorial, Independence, and Labor Days.

Visitors

	Totals	*Reading Room*	*Periodicals Room*
1953:	13,975	9,277	4,698
1952:	13,804	9,391	4,413

Circulation

	Totals	*Intra-mural*[5]	*Extra-mural*	*Books*	*Journals*
1953:	47,788	39,395	8,393	10,558	37,230
1952:	62,804	55,294	7,510	13,055	49,749

Inter-library loans: The library sent 2,616 (1952: 2,308) volumes on inter-library loan to 127 (1952: 108) libraries in 29 (1952: 23) States, D. C., and Canada and has borrowed 2 (1952: 2) volumes from 2 (1952: 1) libraries.

Photostats: 3,438 photostatic prints were furnished on request (1952: 3,013).

Acquisitions and Accessions

Accessioned Acquisitions:

1953: 2,525 volumes (1,732 by purchase; 613 by gift; 180 by exchange). (*Books:* 952; *Periodicals:* 1,573); 90 pamphlets.

1952: 2,025 volumes (1,327 by purchase; 560 by gift; 138 by exchange). (*Books:* 749; *Periodicals:* 1,276); 71 pamphlets.

Non-Accessioned Acquisitions:[6]

1953: 503 Reports (1952: 149).
165 Theses (1952: 839).
160 Miscellaneous items (1952: 61).

Donations

The donors for the past year number 316 (1952: 246). The library is indebted for large gifts of books, pamphlets, and unbound periodicals to the following donors: Dr. S. Bellett; Biological Abstracts; Boston Medical Library; Drs. K. Chouké, R. Friedman; Jefferson Medical College; Drs. R. A. Kern, E. B. Krumbhaar; Lea &

[5] The number of volumes "consulted in the library" includes only those supplied on demand. Readers have access to the bound volumes of periodicals and reference works kept on the shelves in the Reading Room; the Fellows, and occasionally others, by special permission, have access to the book-stacks. There are, therefore, many volumes consulted of which no accurate record can be kept.

[6] As usual, not all the pamphlets, theses, and numbers of various journals listed as received had been checked for keeping or discard at the close of the library year.

Febiger; Pennsylvania Tuberculosis & Health Association; Dr. G. E. Pfahler; Philadelphia County Medical Society; W. B. Saunders Co.; Smith, Kline & French Laboratories; Mrs. A. G. B. Steel & her 3 Sisters (through Dr. Halsey de Wolf and Dr. O. H. P. Pepper); Temple University School of Medicine; Dr. I. J. Wolman.

Various publishing houses, among the large group of corporate donors, have presented volumes as follows: Blakiston Co., 10; F. A. Davis Co., 18; Lea & Febiger, 25; J. B. Lippincott Co., 10; W. B. Saunders Co., 72.

Other individual donors were as follows: S. Adelman; Dr. B. J. Alpers; J. Q. Anderson; Drs. J. H. Arnett, E. Bacon, J. W. Baker; Prof. G. R. de Beer; Prof. W. J. Bell, Jr.; A. S. Berky; Drs. W. R. Bett, W. G. Bowerman, W. N. Bradley, I. Bram, C. C. Briscoe, H. N. Bundesen, W. W. Cadbury; Miss S. Cadwalader; Drs. F. T. Callomon, B. Chance, M. Solis-Cohen, L. P. Coonen, F. Craig, E. J. Cronin, E. T. Crossan; F. Dahl; Drs. D. M. Davis, H. Dittrick, C. M. Downs, G. G. Duncan, W. E. Ehrich, O. S. English; Miss C. R. Flick; Drs. H. F. Flippin, J. F. Fulton, J. L. Gamble; Prof. S. W. Geiser; Drs. J. H. Gibbon, Jr., H. Goldstein, C. A. Hatfield; J. S. Hepburn; Drs. E. Hess, W. N. Hilliard, E. F. Horine; Mrs. R. A. Hunt; Drs. R. H. Ivy, C. Jackson, C. L. Jackson, D. Karnofsky, M. L. Kauffman; E. R. Keedy; Drs. J. V. Klauder, P. C. Kronfeld, W. R. Lange; C. D. Leake; Dr. F. H. Leavitt; M. C. Leikind; Drs. J. J. B. Light, E. Lodholz, J. W. McConnell; W. B. McDaniel, 2d; Drs. D. Macfarlan, H. W. Orr, W. Overholser, T. Parran, M. C. Pease, M. C. J. Pfeiffer, S. X Radbill, D. V. S. Reddy, J. E. Rhoads, J. Lopez Sanchez, J. P. Schaeffer, L. C. Scheffey, H. G. Scheie, P. S. Schidlowsky, W. B. Shelley, H. C. R. Simons, J. Seitchik, J. Stambul, E. A. Strecker, W. E. Stroud, M. Takino, J. M. Thorington, M. Trotter, H. R. Viets, E. Weiss, A. A. Werner, T. K. Wood.

Exchanges

The *Transactions & Studies* was sent, either in exchange or as gift, to 252 organizations.

The library received a number of journal issues through the Medical Library Association Exchange and supplied duplicate journals to other libraries through MLA, USBE, and others.

Theses and dissertations to the number of 165 have been received on exchange from the following European schools of medicine: Universities of Amsterdam, Bern, Copenhagen, Giessen, Jena, Lausanne, Leiden, Liège, Lund, Uppsala, Utrecht.

Work of the Cataloguers

	1953	*1952*
Accessioned items catalogued or recatalogued	952	681
Unaccessioned items and Fellows' reprints catalogued by author or by author and subject	186	190

The Staff

Librarian
Elliott H. Morse

Assistant Librarian
Readers' Service
William K. Beatty

Assistant Librarian
Preparation Division
H. Muriel Hodge

Serials Librarian
Mrs. Elizabeth F. Bready

Secretary and Preparations Assistant
Mrs. Kathryn E. Miragliotta

Assistant Cataloguer
Lillian Ceci

Curator of the Library's Historical Collections
W. B. McDaniel, 2d

Director of the Medical Literature Service
Mrs. Virginia Beatty

Photostat Operator
Margaret Greene

Pages
Dorothy Minton
Julia Carter

Approved:
Jonathan E. Rhoads
Chairman

Elliott H. Morse
Librarian

W. B. McDaniel, 2d
Curator of the Library's Historical Collections

Annual Report of the Committee on the Mütter Museum and College Collections

The Museum

A little publicity has paid dividends as far as the Mütter Museum is concerned, for the year 1953 brought 1752 visitors to view its many treasures. Many came in groups, having made previous arrangements for their accommodation. Among those visiting in a body were pupils from Gillespie Junior High School and the Bok Vocational School, students from the Franklin School of Science and Arts and the Philadelphia Museum School of Art, classes from the Woman's Medical College and student nurses from Lankenau Hospital. It is gratifying to know that the sixteen articles on Museum and College specimens that appeared in *Philadelphia Medicine* during the year were instrumental in bringing many individuals to the Museum. This makes a total of forty-three articles that have been published since October 1951.

Scanning the register for the year, it is learned that visitors came from twenty-four states of the Union and from twelve different foreign countries. Many, in signing, gave only the name of the institution with which they were connected, rather than their home town or city. As there are twenty-three schools, colleges, universities or hospitals represented, persons enrolled there, may well have been from many states and countries not listed in the register.

Those administering the affairs of the Museum are indeed grateful to the many generous donors who continue to supply it with valuable historic material that contributes to its reputation as one of the finest medical museums in the country. The accessions this year were numerous.

Dr. Truman G. Schnabel presented an old chest of medicines that at one time belonged to Dr. William Shippen, Sr. This is of special interest since the previous year a similar chest was presented by Dr. C. Alexander Hatfield, that had belonged to Dr. Shippen's son, Dr. William Shippen, Jr.

An unusual gift, and one that has attracted considerable attention is a miniature model of a therapeutic apparatus made to stretch the human body, invented by Mr. H. W. B. Hausman of Philadelphia, and presented by *Dr. James W. McConnell.*

A Chinese tongue scraper is the gift of *Mr. Harry Buten* presented through *Dr. Samuel X Radbill*, and a bleeding lancet, dated 1732 was a welcome addition from *Mr. M. B. Park*, of Cheltenham.

It is not often that gifts arrive in quantity, but this year it occurred when *Dr. George N. J. Sommer*, of Trenton, New Jersey, arrived with a carton of urinary calculi that he had removed from patients during fifty-five years in the practice of urinary surgery, and another large carton containing forty-one shiny instruments used in this type of operation.

The Sixty-fifth Thomas Dent Mütter Lecture was given December 3, 1952, by Dr. Oscar V. Batson, the title being, *The Veins of Bones: their Connection and Significance.* Dr. Robert P. Glover presented the Sixty-sixth Thomas Dent Mütter Lecture, *The Present Status of Intracardiac Surgery for Mitral and Aortic Stenosis*, on October 7, 1953.

Mrs. Ella N. Wade was reappointed curator and clerk-technician for the year 1952–53, and was in attendance Mondays through Fridays from 9.30 to 1 and from 2 to 4.30, and on Stated Meeting Nights of the College until 8.30 P.M.

R. Philip Custer
Chairman

The College Collections

Donors to College Collections were very generous during 1953. *Dr. J. Monroe Thorington* presented three fine sketches of Dr. and Mrs. R. Tait McKenzie by Violet Oakley, and added

the bronze medals of William Harvey, John Locke and Vesalius to the medical medal collection. He also presented a trigger venesection knife that came from a shop on the main square in Villach, Austria, opposite the house where Paracelsus lived.

Dr. Edward F. Corson, who has already given the college many British War Medals, that had been presented to individuals for medical services, added two more to the collection, together with seven British Decorations and Medals that had been given to Sir Frederick Treves, who served as Surgeon Extraordinary to Queen Victoria, was surgeon to King Edward VII, and, among other things, assisted in the founding of the British Red Cross.

Dr. William G. Leaman, Jr., *Dr. J. Monroe Thorington* and *Dr. Edward F. Corson* joined in the purchase of a collection of medals and badges that formerly belonged to Dr. R. Tait McKenzie. Many of these were presented to Dr. McKenzie for athletic victories during 1889 and 1890. They are of special interest since the College already has many medals modelled by Dr. McKenzie, two of which were recently presented by Dr. Leaman, together with a medal of the International Medical Congress at Washington in 1887.

Dr. Samuel X Radbill also contributed three items to the medal collection.

Two consistent contributors to the College Collections are *Dr. Douglas Macfarlan* and *Dr. Burton Chance*. Dr. Macfarlan added six foreign bodies that had been removed from the ear, to the otologic exhibit, a transistor that this year replaced the vacuum tube in hearing-aids, the first hearing test record, that was used in the Lennox Avenue School for the Deaf in New York, and a medicine spoon used about 1890. Dr. Chance presented eleven ophthalmic instruments, a cataract that had undergone calcareous degeneration, a cast of Hutchinson's teeth, and he increased by four the ophthalmoscope display.

The acquisition of pathological material is rare, but in 1953 *Dr. Theodore F. Bach* presented three arthritic specimens, and *Dr. Samuel R. Skillern, Jr.* donated face sections showing sinus abnormalities found by R. H. and S. R. Skillern while sectioning one hundred heads in 1909. These specimens are displayed in the Museum, but are catalogued in College Collections so that they may be removed for study if requested.

The College possessed no bronchoscopes until Dr. Louis H. Clerf, in 1952, presented two of these instruments. This year the *George P. Pilling & Son Company* gave the College a standard Jackson bronchoscope.

Instruments outnumber all other donations. An old scarificator from the Kensington Dispensary for Tuberculosis, presented through *Dr. William P. Lampe*, is now a College possession, and *Dr. Samuel X Radbill* added an abdominal trocar.

The oldest microscope in the College Collection, with the exception of the replica of Leeuwenhoek's, is a Culpeper-Scarlet type, dated about 1750, that *Dr. Balduin Lucké* sent to the College this year.

From *Miss Jessie Dobson*, Recorder of the Museum at the Royal College of Surgeons, London, the College received an excellent plaster plaque of John Hunter, one of several copies which Professor Wood Jones had had made from an original by John Tweed. The art collection was further augmented by the acquisition of three oil portraits; one of *Dr. Richard A. Kern*, President of the College, by Harry Moskowitz, another of Dr. John Thompson Hodgen, teacher of physiology and anatomy and Dean of the St. Louis Medical College, and also a former Associate Fellow of the College of Physicians, presented by *Dr. Stuart Mudd* and *Mr. Raoul Pantaleoni*, and a third of Dr. Roland G. Curtin, one of the first cardiologists, painted by William T. Smedley, and presented by his daughter *Miss Mary C. Curtin*.

Three portraits were restored during the year by Mr. Frank Ireland, namely those of Dr. John Ashhurst, Dr. John Redman and Dr. David Hayes Agnew.

Mrs. Wade continued as custodian of College Collections for the year 1952–53.

R. Philip Custer
Chairman

Annual Reports of the Sections

General Medicine

The customary seven meetings were held during the year, the names of 48 Fellows and 27 guests appearing on the programs. Abstracts of 24 of the 28 presentations will be found in the *Transactions & Studies*. The attendance included an average of 80% of the Section's membership of 162.

Charles M. Thompson
Clerk

Medical History

The number of Fellows contributing to the support of the Section each year has shown a steady gain. 139 have paid their dues during 1953. At least some of this increase in membership must be due to a growing desire on the part of the Fellows of the College to further encourage the study of medical history in Philadelphia. The College of Physicians of Philadelphia with its vast and growing historical resources is looked upon more and more as the natural center for research and teaching of the history of medicine in Philadelphia. It is hoped that some day the Section on Medical History can lead the way in establishing here, a chair, which will attract a suitable individual, preferably an M.D., with a flair for medical history and a talent for teaching, "and the willingness to get rich slowly or not at all", which will receive the support of the medical schools, practicing physicians and other interested parties as a whole. With adequate preliminary training, such an individual could profitably take care of the teaching needs of all the medical schools of Philadelphia as well as hold seminars for the physicians of this city and for other historians organizing original work in the history of medicine.

In order to stimulate the interest of the coming generation of physicians, the Section on Medical History this year inaugurated a prize of $100 for the best essay in medical history submitted by October 1, 1954. All students of the five medical schools of Philadelphia are eligible to compete. A prize committee consisting of Drs. Herman Beerman, Pascal F. Lucchesi and Philip F. Williams was appointed by the Chairman of the Section. This committee will review all the essays submitted and decide on the one to be recommended to the Executive Committee of the Section for the prize award. The following rules were drawn up and distributed:

"The Section's purpose in offering an award of $100 for the best essay on the history of medicine submitted by a student in any one of the medical schools of Philadelphia is to help stimulate in the students an interest in, and some knowledge of, the life-process of medicine itself, to the end that, as eventual practitioners, they may work more effectively in the wider perspective attained, and with greater personal satisfaction.

"The student is advised that participation in the contest must not usurp time that should be devoted to the formal curriculum; rather, that the project should be a spare-time one, linked, if possible, to some aspect of the technical training he is engaged in. Instructors in a course in which the student is particularly interested might be asked, for instance, to suggest small areas in the historical development of the subject which might usefully receive further attention.

"Whatever the topic selected, it is anticipated that the student will obtain practical training in his use of historical sources, the organization of his material, and the final preparation of a documented paper that will benefit him in the practice of his profession.

Rules

1. Essays submitted must be typewritten or written in clearly legible hand, on one side of the sheet only, with wide margins and double space between lines. The length should be ap-

propriate to the topic and the treatment selected.

2. Essays must be accompanied by A.) a statement from the dean's office that the author is a duly enrolled student in the school; B.) a statement by the author that the paper has not been published, and that priority in rights of publication is accorded to the *Transaction & Studies of the College of Physicians of Philadelphia.*

3. Essays must contain numbered citations in the text to an appended, correspondingly numbered list of full bibliographic references. The citations should be used whenever important statements of fact or interpretations have been drawn from the sources consulted. The bibliographic references follow the style used by the *Journal of the American Medical Association.*

4. Essays and correspondence should be addressed to the Section on Medical History, Essay Contest, College of Physicians of Philadelphia, 19 So. 22d St., Philadelphia 3, Pa., on or before October 1, 1954.

October, 1953 SAMUEL X RADBILL, M.D.
Clerk of the Section"

Three stated meetings have been held during the winter of 1953, all of which were well attended. The programs have already been published in the *Transactions & Studies* of the College. One of the meetings was arranged with the financial and inspirational support of the Woman's Medical College of Pennsylvania to present the Kate Hurd Mead Class of 1888 Lecture in Medical History. This is the fourth successive year that we have had the happy experience of combining our efforts to present to this city an outstanding guest lecturer on a topic in medical history. Acknowledgment should here be made of the help and encouragement in making these lectures possible that come from Dean Marion Fay.

Because invited guests have appeared on the programs, a dinner preceded each meeting. To Dr. and Mrs. Wm. G. Leaman, Jr., again go our thanks for their delightful cocktail parties. At these parties we are afforded not only pleasant social contacts but also gain from the opportunity for more intimate discussion on topics allied to the medical humanities.

The course of six weekly lectures by Drs. Temkin and Shryock of the Johns Hopkins University Institute of the History of Medicine to the students of the five medical schools of the city was repeated. The attendance was good with an over-all count of 1109. Considering the fact that attendance at these lectures is purely voluntary on the part of the students who are in no way afterward held accountable for what they learn or do not learn; that the lectures are given outside the regular curriculum time and at a distance from most of the schools so that a distinct effort to come has to be made on the part of the students, I feel that since the students come so willingly, we are fully justified in continuing to expend the thought, time and effort required to enable these lectures to be presented. In the final analysis, however, it is the financial support annually provided by the medical schools themselves which makes possible this opportunity in medical culture for the students. That there are others, too, who enjoy the liberality of the Philadelphia medical schools, is evident from the liberal sprinkling of the students' elders throughout the audience at each lecture.

As in the past, Dr. McDaniel and Mrs. Wade have prepared timely exhibits from the resources of the College Library and Mütter Museum before each lecture. Before and after each meeting, clusters of students were seen absorbed with interest studying these rare books and instruments basic to the development of our profession and seeing at first hand how the past became the present, leading to the future.

The Clerk of the Section, as Lecturer in the History of Pediatrics, in the Graduate School of Medicine of the University of Pennsylvania, presented a course of six lectures in the history of pediatrics at the College utilizing again the resources of our institution to good advantage. A lecture was also given as part of a course in the history of dermatology to the Graduate

students in the Department of Dermatology. To Mr. Elliott H. Morse and the administrative staff of the College go our thanks for considerable aid in helping us to set up these lectures.

The Clerk of the Section also serves at present, as Secretary of the American Association of the History of Medicine and in this capacity attended the annual meeting of this national organization at Columbus, Ohio, in May, 1953. He also attended, unofficially, the 13th International Congress of the History of Medicine at Nice, France, and the Annual Meeting of the German Society for the History of Medicine and Technology at Schweinfurt, Germany, in September, 1952. Serving on the Osler Memorial & Blockley Historical Committee, he helped to prepare and organize a program for the ceremonies in connection with the presentation by Wyeth Laboratories, Inc., of the Osler painting by Dean Cornwall to the Philadelphia General Hospital; prepared an exhibit of medical bookplates for the Milwaukee Art Institute; reviewed various books bearing on the history of medicine for several publications and assisted in the preparation of several manuscripts.

A contribution of $100 was also made by the Section to help defray the travelling expenses of the library's Curator of Historical Collections in order to enable him to attend the First International Congress on Medical Librarianship in London, England, at which he had been invited to make an address.

The records of the Section during the years 1948 to 1953, inclusive, were added to those already on deposit with the librarian of the College of Physicians of Philadelphia for preservation and safe keeping.

An invitation by the President of the University of Cincinnati and the President of the Cincinnati Academy of Medicine to attend The Ceremony on the occasion of the 100th anniversary of the death of Daniel Drake, May 27, 1952, at Cincinnati, was appropriately acknowledged.

Samuel X Radbill
Clerk

Ophthalmology

The total membership in the Section was 65, of whom 64 paid dues. There was an average attendance of 100 at the seven meetings.

The Sixteenth Annual de Schweinitz Lecture was delivered by Alan C. Woods, M.D., of Baltimore, on November 19th.

The Zentmayer Prize was awarded to Robert H. Bedrossian, M.D., for his paper, *Retrolental Fibroplasia and Its Relationship to Oxygen.*

M. Luther Kauffman
Clerk

Otolaryngology

The Section held five meetings at the College, and a joint one, in New York, with the Section on Otolaryngology of the New York Academy of Medicine. Attendance averaged about 19. The Section has 59 regular, and 7 honorary, members. Twenty-three Fellows and seven guests participated in the programs.

Benjamin H. Shuster
Clerk

Section on Public Health, Preventive and Industrial Medicine

Two meetings were held. The first, in April, was devoted to problems of world health and presented speakers from Norway, Western Germany, India, Chile, Korea, and Brazil. There was a good attendance and lively discussion after the presentations. The program of the second meeting, in October, had as its feature a paper on the Montefiore Hospital (N. Y.) home care program. This led to discussion of the requisites for such programs, of the program undertaken by the Visiting Nurse Society of Philadelphia, and of the application of such programs to specialized public health problems such as tuberculosis.

The Section had 57 members.

Robert V. Cohen
Clerk

Memoir of Edwin E. Graham (1864–1953)*

By EDWARD L. BAUER

THE last two decades of the nineteenth century were the scene of a renaissance that paved the way for our modern more scientific approach to the practice of medicine. Surgery had been given a new impetus by the work of Pasteur and Lister, medicine by Osler and the specialties though as yet ill defined were beginning to take form and substance.

During this period the Jefferson Medical College graduated Edwin E. Graham in the class of 1887. He had been well prepared for his medical studies first in his native city of Philadelphia at the Episcopal Academy and later at Phillips Exeter. He received his Bachelor of Arts degree in 1884 at Harvard University.

Dr. Graham served his internship and residency at the Philadelphia General Hospital. After his residency he studied at the German Universities of Göttingen, Munich and Berlin where he was under the tutelage of Henoch. While he visited Trinity College in Dublin from which his father, Archibald Hunter Graham, had graduated in medicine there is no evidence that he tarried there. Upon his return he became affiliated with the Out Patient Department of Jefferson Hospital.

His interest lay in the direction of the care of the sick child. While many men had become interested in this field from the time of Soranus no serious specialty had been developed. Dr. Graham along with other young men throughout the United States pioneered to establish such a specialty on a firm basis. When they started there was no knowledge of the real processes of growth and the word "development" might have been left out of the dictionary as far as the metamorphosis from infancy to adult life was concerned. The sick child was their immediate problem. They were handicapped by the prejudices of obstetricians and the inability of the general run of medical men and laity to recognize the difference between the illnesses of children and similar conditions in adults.

In the papers that he wrote Dr. Graham devoted himself to clinical research in symptomatology and therapeutics. This is evident in his contributions to Hare's "System of Practical Therapeutics" and Wilson's "American Textbook of Applied Therapeutics". He was not only a contributor but was on the editorial board of the *American Journal of Diseases of Children.*

In 1892 the specialty received a forward impetus when some medical schools gave recognition to the diseases of children as a specialty. It was not as yet too wholehearted. In that year Dr. Graham was made Clinical Professor of Diseases of Children at Jefferson Medical College. It was several years later, in 1904, that Jefferson established an independent department of pediatrics and Dr. Graham was appointed Professor of Diseases of Children in which capacity he served until 1926. At that time he was made Professor Emeritus of Diseases of Children. In the meantime he served many years as Pediatrist to the Philadelphia General Hospital and the Vineland Training School in New Jersey. During this period, in 1916, he wrote a pediatric textbook.

Professor Graham's interest in pediatrics was not confined to the immediate environs of the Jefferson Medical College. He was one of the early members of the American Pediatric Society of which he was president for one year. At that time his presidential address was the first paper published in the United States dealing with "Deaths in Children from Infectious Diseases during the First Five Years of Life". Later he presented to this organization a paper that was both new and outstanding on "Foreign Bodies in the Air and Food Passages". As chairman of the Section on Pediatrics

* Prepared and published at the request of the Council of the College of Physicians of Philadelphia.

of the American Medical Association of which he was a Fellow his paper was another first on the subject, "Infant Mortality". He was chairman of the Section on Pediatrics of the Medical Society of the State of Pennsylvania.

Locally Professor Graham was a Fellow of the College of Physicians of Philadelphia and the Philadelphia Pediatrics Society and in the latter he served a term as president. He sought no honors but was always ready to respond with any service he could render when requested to do so. He attempted along with Rotch, Wescott, Chapin and some others of the New York pediatrists to rescue artificial feeding of infants from the throes of the superstitious and the traditions of the midwife. These men vied with each other in an attempt to modify cow's milk so that it would match human milk in structure. It resulted in the percentage system which held the country in its grip for a decade and a half. He saw clearly the need for meticulous cleanliness in milk and in the preparation of the formula. He was active in formulating the standards of certification of milk and later pasteurization. He was actively engaged in the battle for the tuberculin-testing of cows.

A few of the neophytes in this scientific day of medical practice are wont to look patronizingly at a life like Professor Graham's even as the young aviator looks out of his jet plane and sneers at the horse and buggy. But to such men as Professor Graham the profession can look with admiration and awe for they made a light where there was darkness and made the path of progress easier for their followers.

In his sixty odd years of practice his accomplishments in the art of medicine endeared him to those who sought his advice even to succeeding generations. His home life was idyllic. The interpendence of himself and his wife was complete. The devotion of his two daughters, now Mrs. Henry B. Robb, Jr. and Mrs. Edwin A. Bacon, was another happy factor in this domestic picture. Their loving care was a great boon at the time of the tragic accidental death of his wife, nee Lorraine Goodrich.

Professor Graham was active in the Presbyterian Church. He was well known and well beloved in this denomination and was associated in many good works with the late John Wanamaker in Bethany Church in Philadelphia.

In 1950 Professor Graham was honored by Jefferson Medical College with the degree of Doctor of Science. In the next year because of infirmities he gave up active practice. On June 19th, 1953 while visiting his daughter, Mrs. Bacon, in Madison, Virginia, Professor Graham passed on to rejoin his wife and receive the greatest reward of service that can be attained by a strong devoted Christian gentleman who has served his fellowman well.

"Inasmuch as ye have done it unto the least of these My brethren, ye have done it unto Me."

Memoir of Warfield Theobald Longcope (1877–1953)*

By FRANCIS D. W. LUKENS

WARFIELD T. LONGCOPE, an Honorary Fellow of the College, was born in Baltimore, Maryland, on March 29, 1877, and died at his country home, Cornhill Farm, Lee, Massachusetts, on April 25, 1953.

After preparatory schooling in Baltimore, he received his Bachelor's Degree from Johns Hopkins at the age of 20. In the same year he entered the new Johns Hopkins Medical School and graduated in 1901 in its fifth class. As a medical student, he came under the influence of Mall, Welch and Osler and as a result, had contributed several papers in the fields of pathology and bacteriology by the time he graduated. He left Baltimore at the age of 24 to pursue these studies as resident pathologist and later as Director of the Ayer Clinical Laboratory at the Pennsylvania Hospital (1904–1911). Here Simon Flexner furthered his interest in immunology and he enjoyed the association with David Edsall, Theodore Janeway, and others. At this time clinical investigation was in a primitive stage, from the present point of view. Dr. Longcope made the first blood cultures ever performed at the Pennsylvania Hospital. In reference to these, he said: "venepuncture for bacteriological culture was such an innovation that as a daring novice trembling with apprehension, these cultures were performed." In Philadelphia he developed his interest in immunology and in the etiology of various diseases. One of these was Bright's disease, the study of which led him into the field of serum sickness and the immunological reactions found in that condition.

In 1911 Dr. Longcope left Philadelphia to become Associate Professor of Medicine at Columbia University. Three years later at the age of 37, he was appointed Bard Professor of Medicine and Director of the Medical Service of the Presbyterian Hospital, where he remained until 1921. During these 10 years he carried out a number of clinical and immunological investigations. In 1917–19 he was on leave of absence as a consultant for the American Expeditionary Forces in Europe.

In 1921, he left Columbia University and entered practice in New York City. In 1922 he returned to Baltimore and became Professor of Medicine and Physician-in-Chief at the Johns Hopkins Hospital and Medical School. In spite of the pressure of teaching and administration, he devoted part of almost every day to his laboratory where his kind encouragement and stimulating influence fell upon a succession of fortunate junior men. Even during World War II, after he had passed the age of 65 and his staff was depleted by enlistment, he succeeded in both directing and sharing in experimental and clinical investigations on the effect of British Anti-Lewisite. During his years at Hopkins he wrote fundamental articles in many fields including:—Hodgkin's disease, allergy and serum sickness, glomerulonephritis, sarcoidosis, atypical pneumonia and others.

Dr. Longcope exerted an unusual and outstanding influence on American medicine. He was a superb clinical teacher who brought to either the classroom or the bedside a beautifully ordered fund of information about disease processes. This was a blend of personal experience and wide reading. He avoided anything spectacular but drilled his staff in precise, methodical and well ordered procedures. As might be expected, such qualities were best taught by his example. His rare enthusiasm, scholarly criticism and unending generosity toward all the junior members of his staff made it the greatest privilege to serve with him.

* Prepared and published at the request of the Council of the College of Physicians of Philadelphia.

The greatest testimonial to his influence upon younger men is to be found in the list of his former residents and junior staff who occupy prominent positions in the world of medical education.

"The Professor's" influence was also exerted by his active participation in numerous medical and scientific societies. These need not be recorded here but he served as President of the Association of American Physicians and was the recipient of its Kober Medal in 1948. He was President of the Society for Clinical Investigation in 1919 and became President of the Board of Scientific Directors of the Rockefeller Institute in 1939. He was a member of the National Academy of Sciences and of the Société des Hôpitaux, Paris, an Honorary Fellow of the Royal College of Physicians of England and of the Scandinavian Congress of Internal Medicine. He received honorary degrees from several universities including his Alma Mater.

Longcope was married in 1915 to Janet Percy Dana who made their happy home a constant center of hospitality to successive groups of Hopkins students and house officers.

In closing, all of those who knew Dr. Longcope are deeply grateful for the opportunity which this rare companionship afforded. In our hearts he will always hold a place of high esteem and sincere affection.

Memoir of B. B. Vincent Lyon (1880–1953)*

By MARTIN E. REHFUSS

THE death of Dr. B. B. Vincent Lyon removes from our ranks one of the great gastroenterologists and internists of whom America may well be proud. He died suddenly in Washington, D. C., May 20, 1953, aged 73, or coronary thrombosis.

Dr. Lyon was born in Erie, Pa., March 20, 1880, the son of George Armstrong and Rose (Vincent) Lyon. His earlier education was spent at the Lawrenceville Preparatory School, 1889, and Williams College (A. B.) 1903, Sc.D. 1931, and received his medical degree at the Johns Hopkins Medical School in 1907. He served his internship at the old German (Lankenau) Hospital and later formed the first Gastrointestinal Clinic there in 1910. After that he was associated with the Jefferson Medical College where he founded the out-patient Gastrointestinal Clinic which he continued until the date of his retirement in 1946. This clinic was a famous centre for all those interested in biliary tract disease. He was appointed Demonstrator of Medicine in 1910; he was steadily advanced until he became Clinical Professor of Medicine on his retirement. He served in the Medical Corps of the United States Navy during World War I, 1917–1918 at the Naval Base Hospital at Brest and with the Marine Corps and U. S. Army in France.

He is best known by his pioneer work on the biliary tract and by the introduction of non-surgical or diagnostic biliar drainage by means of which new light was thrown on normal and abnormal biliary tract function. By means of this procedure he described the color sequence and characteristics of the different bile fractions after stimulation through the duodenal tube. Those of us who were active during that period will recall the controversy which that early publication in 1919 induced. Lyon claimed that the dark "B" fraction was predominantly gallbladder bile. The controversy over this subject and the introduction of a new method for the investigation of the biliary tract proved to be a tremendous stimulus in a field which previously had been so largely surgical. Lyon demonstrated, beyond all question, the feasibility of studying the biliary tract in this fashion. The first two great principles—the demonstration of color sequence and the demonstration of normal and abnormal cytology—are permanent additions to our knowledge of this field, and perhaps the future will amplify them by the contributions of biologic chemistry in this field.

Stimulated by his early cytologic studies on gastric sediments and their interpretation, his interest naturally led him to the biliary tract. Not only did he prove that "B" bile was predominantly gallbladder bile, but his numerous contributions reveal every detail of the microscopic studies of this subject. His Atlas on biliary drainage microscopy emphasizes the cytologic differences encountered in various forms of biliary tract disease and his many contributions reveal various phases of this fascinating subject—the cytology of the bile, the bacteriology of bile, the phenomena associated with catarrhal cholangitis, cholecystitis, jaundice, duodenal parasitosis. It was not long before he became interested in non-surgical duodenal drainage as a therapeutic weapon, not only in biliary tract but in liver disease. If his zeal as a crusader at times produced over-optimism, it is nevertheless true that the succeeding years have amply demonstrated that there is a definite field in which this method is invaluable. He was the first, I believe, who was able to demonstrate that in certain selected cases a positive cholecystogram might be changed into a negative by judicious and repeated drainage. I have always thought that had his health permitted, he would have

* Prepared and published at the request of the Council of the College of Physicians of Philadelphia.

continued the correlation of tube and x-ray technic and operative findings, which today are the most effective methods at our disposal for throwing light on the biliary tract. His volume on Non-Surgical Drainage of the Gall Tract (Phila. Lea and Febiger, 1923) is a classic.

Even though these books were published some decades ago, the student of today will nowhere find more thorough and elucidating information regarding the diagnostic value of duodenal drainage.

He was a brilliant speaker, a confirmed enthusiast in his chosen field and an indefatigable worker. He was the recipient of many honors and became president of the American Gastroenterological Association in 1934. His interest in that national institution never flagged. He received the Julius Friedenwald medal in 1950. Even though ill health followed him in later years, his flaming courage and drive never deserted him during the great years when he was carrying on his epoch making work. Gastroenterologists everywhere and the American medical profession have lost a valiant spirit and one who has contributed so richly to his chosen subject. Many of us who knew him well will miss his indomitable spirit and his unflagging energy.

Transactions of the Sections

SECTION ON GENERAL MEDICINE

25 May 1953

The Incidence of Diabetes in Diffuse Pancreatic Disease. C. Robert Tittle, Jr.*, M.D. (Discusser: Joseph T. Beardwood, Jr., M.D.) (*Abstract 1, below*)

Acute Upper Gastro-Intestinal Hemorrhage. Donald Berkowitz*, M.D., and Irvin Sussman*, M.D. (Discusser: C. Wilmer Wirts, M.D.) (*Abstract 2, below*)

Susceptibility to Thrombophlebitis. Meyer Naide, M.D. (Discusser: William G. Leaman, Jr., M.D.) (*Abstract 3, below*)

Some Experiences in Ballistocardiographic Changes Following Cardiac Surgery. William Likoff*, M.D. (Discussers: Truman G. Schnabel, Jr.*, M.D., Peter Quo*, M.D., and Edward W. Bixby, Jr.*, M.D.)

26 October 1953

The Thyrotoxic Remnant. John H. Nodine*, M.D., and William H. Perloff, M.D. (Discusser: Robert Robbins, M.D.)

Presacral Air Injection in the Diagnosis of Abdominal Lymphoma. George T. Wohl, M.D., Ralph Myerson*, M.D., Abraham M. Frumin*, M.D., and Paul Rouse*, M.D.) (Discusser: Harold J. Isard, M.D.) (*Abstract 4, below*)

Acholia: White Bile in the Common Duct, with Clinical Recovery. Herbert R. Hawthorne, M.D., and Julian A. Sterling, M.D. (Discusser: Henry J. Tumen, M.D.) (*Abstract 5, below*)

Progress Report on the Interpretation of Protein Bound Iodine Measurements in Serum. F. William Sunderman, M.D., and F. William Sunderman, Jr.* (Discusser: Edward Rose, M.D.) (*Abstract 6, below*)

23 November 1953

Untoward Reactions Associated with Apresoline Therapy. M. August Lindauer, M.D., and Joseph H. Hafkenschiel, M.D. (Discusser: John Lansbury, M.D.) (*Abstract 7, below*)

Allergy to Foods Containing Sulfur-amino Acids, Especially Methionine: Case Report and Clinical Study. Louis Tuft, M.D., L. N. Ettelson*, M.D., and H. Schwartz*, B. S. (Discusser: Merle M. Miller, M.D.) (*Abstract 8, below*)

A Cool Box to Measure Blood Flow in Peripheral Arterial Disease. Raymond Penneys, M.D. (Discusser: Daniel J. Marino*, M.D.) (*Abstract 9, below*)

Cases Returning to Former Occupations Following Myocardial Infarction. William D. Stroud, M.D. (Discusser: Joseph A. Wagner, M.D.) (*Abstract 10, below*)

SECTION ON MEDICAL HISTORY

Sixth Series of Lectures for Medical Students, 1953

I. Introductory: The Meaning and Values of Medical History. Richard H. Shryock*, Ph.D. (12 Oct.)

II. Classical and Medieval Medicine. Owsei Temkin*, M.D. (19 Oct.)

III. Renaissance Medicine. Dr. Temkin. (26 Oct.)

IV. 17th and 18th Century Medicine. Dr. Temkin. (2 Nov.)

V. 19th and 20th Century Medicine. Dr. Shryock. (9 Nov.)

VI. Social Aspects of Medical History. Dr. Shryock. (16 Nov.)

SECTION ON OPHTHALMOLOGY[1]

22 October 1953

Traumatic Arteriovenous Aneurysms with Bilateral Sixth Nerve Palsy. Edmund Spaeth, M.D., and Joseph Yaskin, M.D.

Some Aspects of Torsion. J. Van Dyke

* By invitation.

[1] Abstracts of the presentations at this Section customarily appear in the *American Journal of Ophthalmology* and the *A.M.A. Archives of Ophthalmology*.

Quereau*, M.D. (Discusser: Francis H. Adler, M.D.)

Relationship Between Corneal and Total Astigmia. Edwin Forbes Tait, M.D. (Discusser: Alfred Cowan, M.D.)

19 November 1953

The Pathogenesis and Treatment of Ocular Tuberculosis. Alan C. Woods*, M.D. (*Sixteenth Annual de Schweinitz Lecture*)

17 December 1953

Malignant Glaucoma. P. Robb McDonald, M.D.

Surgical Management of Intermittent Exotropia. Robert D. Mulberger*, M.D. (Discusser: William E. Krewson, 3d, M.D.)

Experimental Intraocular Infection with Mumps Virus. H. P. Kirber*, M.D., and Marie W. Kirber*, M.D. (Discusser: Werner Henle*, M.D.)

SECTION ON OTOLARYNGOLOGY[2]

18 November 1953

Sarcoid Sinusitis. Bernard J. Ronis. M.D. (Discusser: Robert V. Cohen, M.D.)

Allergy of the Ear. William J. Hitschler, M.D. (Discusser: Merle M. Miller, M.D.)

Cavernous Tissue of the Nose. Oscar V. Batson, M.D.

16 December 1953

Malignancy of Sphenoid. Austin T. Smith, M.D.

Thyroglossal Duct Fistula with Lateral Opening. Floyd J. Putney, M.D.

Eosinophilic Granuloma of Frontal Bone. Benjamin H. Shuster, M.D., and Thomas F. Flynn*, M.D.

Carcinoma of Both Tonsils. Louis E. Silcox, M.D.

Necrosis of Mandible Following Peritonsillar Abscess. Harry P. Schenck, M.D., and Allan R. Shuster*, M.D.

SECTION ON PUBLIC HEALTH, PREVENTIVE AND INDUSTRIAL MEDICINE

8 October 1953

The Montefiore Hospital Home Care Program. George A. Silver*, M.D. (Discussers: James P. Dixon, M.D., and Arthur M. Rogers, M.D.)

Abstracts

Abstract 1

The Incidence of Diabetes in Diffuse Pancreatic Disease. C. R. Tittle, Jr., M.D. Interest in this subject has been stimulated by the opportunity to observe the diabetic state accompanying diseases characterized by the destruction of pancreatic tissue. Hemochromatosis provides a clear example of production of diabetes by gradual destruction of the pancreas by a known agent. Needle biopsy of the liver is now a well established diagnostic aid in this disease and should be employed more often in attempting to discover the cause of insulin resistant cases of diabetes. Several cases of total pancreatectomy in man with appreciable survival periods are now in the literature. Such cases are interesting in having a fairly uniform insulin requirement of about 40 units per day. Two peculiarities of the diabetic state following pancreatectomy, namely, relatively low insulin requirement and marked insulin sensitivity, have been attributed to the loss of a hyperglycemic factor presumably produced by the alpha cells of the pancreas. Cancer of the pancreas and abnormalities of carbohydrate metabolism occur together more frequently than can be accounted for on the basis of chance. Using the glucose tolerance test, Berk found abnormal curves in 7 of 9 cases tested, and a subsequent survey of 90 cases of pancreatic malignancy revealed impaired

[2] Abstracts of the presentations at this Section customarily appear in the *A.M.A. Archives of Otolaryngology.*

glucose tolerance in 86% and fasting hyperglycemia in 60%.

Recent progress in the diagnosis of pancreatitis has been marked due to the employment of a variety of new pancreatic function tests and the increasing evidence that mild cases of acute pancreatitis are not rare, especially Comforts' report of the entity which he terms chronic relapsing pancreatitis. A review of 27 unselected cases of acute pancreatitis at Graduate Hospital, revealed that 9 cases showed elevated blood sugar during some stage of the acute disease and permanent diabetes developed in 4 of the 9 cases. Sixteen cases diagnosed as chronic pancreatitis, at the same hospital, were also reviewed. Ten of the 16 showed some disturbance in carbohydrate metabolism and 6 became permanently diabetic. Three cases of pancreatic calcinosis are included in the group, all of whom were diabetic. Review of the 12 cases classified as permanently diabetic revealed no antecedent diabetic history in any case, and a family history of diabetes in only one. These 12 cases represent an incidence of approximately 28% of diabetes mellitus following a small series of acute or chronic pancreatitis.

Abstract 2

Acute Upper Gastro-Intestinal Hemorrhage. Donald Berkowitz, M.D., and Irvin Sussman, M.D.

450 cases of acute upper gastro-intestinal hemorrhage seen during the past 5 years at Hahnemann Hospital are analyzed. Seventy-six per cent (342 cases) were due to peptic ulcer (274 duodenal, 47 gastric, 12 marginal, and 9 gastric and duodenal). There were 37 cases of esophageal varix bleeding, 21 cases of miscellaneous causes, and a large group of 50 patients in whom no cause for the bleeding could be found.

The over-all mortality for the entire group was 13%. There was a 4.6% mortality in the medically treated ulcer patients, and a 10.8% mortality in the surgically treated group. Esophageal varix bleeding was attended by a high mortality of 64%.

Various factors were found to be associated with a higher mortality in hemorrhage from peptic ulcer: 1) the age of the patient, 2) gastric ulcers, 3) hemetemesis, 4) the height of the red cell count, 5) the presence of shock, and 6) other complicating diseases.

Intelligent management of the patient with acute gastro-intestinal bleeding can only be accomplished by a systematic and orderly approach which takes into account all the various factors which contribute to a less favorable prognosis.

Abstract 3

Susceptibility to Thrombophlebitis. Meyer Naide, M.D.

Attempts to develop a test for determining which patients might be predisposed to thrombophlebitis have the defect that they must be applied to many patients who will never develop thrombophlebitis in order that the small percentage (1%) who develop it may be detected. A group of patients have been studied who have already shown a predisposition, namely, patients who have had thrombophlebitis. From this group of patients we learned that previous thrombophlebitis is no contraindication to further pregnancy or surgery, provided that certain prophylactic measures are taken against thrombophlebitis. Only rarely does a patient seem to have some inherent predisposing factor. The fact that thrombophlebitis did not occur in most of these patients in further pregnancies and operations suggests that something occurred or was present at the time of the episode of thrombophlebitis that was not repeated later. A group that behaved somewhat differently was the group with spontaneous venous thrombosis, not post-partum or post-operative. In these patients pulmonary embolism is not uncommon. Furthermore, recurrence is much more likely in patients with spontaneous venous thrombosis. In this group careful watching or post-operative anticoagulants may be necessary if the patient requires further surgery. All patients who have had thrombophlebitis

previously and require further surgery or are post-partum should have the legs elevated and examined daily.

Abstract 4

PRESACRAL AIR INJECTION IN THE DIAGNOSIS OF ABDOMINAL LYMPHOMA. George T. Wohl, M.D.; Ralph Myerson, M.D.; Abraham M. Frumin, M.D.; and Paul Rouse, M.D.

A brief historical review of the technique of retroperitoneal air injection was presented with particular emphasis on the newer method introduced by Rivas of using a presacral route of injection. The anatomy of the retroperitoneal spaces was discussed and illustrations, by slide, of the appearance of the normal contrast roentgen study following injection of approximately 1000 cc. of air through the presacral route were presented. The technique had been used in four patients presenting the differential diagnostic problem of mass lesions of the midline retroperitoneal structures. By means of this technique, it was possible to arrive at a definitive diagnosis in these four patients. One of these was a patient with backache of unknown etiology presenting a large radiosensitive midline nodal mass that subsequently, by lymph node biopsy, was proved to be due to Hodgkin's Disease. A second patient was found, by the use of combined presacral air injection and body section roentgenology of the midline abdominal structures, to have enlarged abdominal nodes secondary to lymphosarcoma. A third patient was found to have metastatic nodes from a primary seminoma that had been removed three years prior to this study. A fourth patient was found to have metastatic nodes from a known teratocarcinoma of the testis removed approximately three weeks prior to this admission. The finding of the metastatic nodes was confirmed by surgical node exploration.

The use of the combined presacral air study with body section roentgenology of the midline abdominal structures is suggested where there is a problem of differential diagnosis involving these structures.

Abstract 5

ACHOLIA: WHITE BILE IN THE COMMON DUCT, WITH CLINICAL RECOVERY. Herbert R. Hawthorne, M.D., and Julian A. Sterling, M.D.

Acholia has been considered as that state wherein (liver) bile does not appear in the bile ducts. It can occur in the presence of obstructive jaundice whether it be inflammatory (cholangitis or hepatitis), calculous or neoplastic. Presence of white bile in the common duct (or the absence of bile therein) indicates hepatic insufficiency. This usually prophesies a subsequent fatality.

Acholia does not necessarily carry a poor prognosis in patients who have benign obstruction to the ducts or in those who have hepatitis. It is important to correlate urine urobilinogen with serum bilirubin levels over consecutive days in order to determine, for example, that a lowered serum bilirubin level actually is associated with the appearance of bile in the intestinal tract.

An indication for early surgical intervention in a patient with obstructive jaundice exists when the serum bilirubin is stabilized or decreasing in the absence of positive proof that bile is reaching the intestinal tract. Drainage of the bile passages under such conditions is essential in order to permit an opportunity for the hepatic cell function to be restored.

Two patients are reported who had chronic calculous obstruction to the common bile duct. They recovered from a severe form of hepatic insufficiency manifest by "acholia." The necessity for suspecting the presence of this type of liver failure is emphasized.

Abstract 6

PROGRESS REPORT ON THE INTERPRETATION OF PROTEIN BOUND IODINE MEASUREMENTS IN SERUM. F. William Sunderman, M.D., and F. William Sunderman, Jr.

The estimation of the concentration of protein bound iodine in serum furnishes valuable information regarding the concentration of thyroid hormone in the circulation. Duplicate analyses for protein bound iodine were made on 65 adult

blood donors, by our modification of the alkaline fusion method of Barker and Humphrey. The mean value obtained was 5.0γ per 100 ml, SD ±1.0, with a range of 2.9–7.9γ per 100 ml. In 56 cases giving definite clinical signs of hyperthyroidism, the concentrations of PBI in serum ranged from 6.5 to 29.0γ per 100 ml, and in 15 cases clinically diagnosed as suffering from hypothyroidism, the concentrations of PBI in serum ranged from 0.4 to 3.4γ per 100 ml.

The measurement of PBI has been found especially useful in the diagnosis of masked hyperthyroid states, i.e., those conditions in which the clinical signs and symptoms of thyrotoxicosis are absent or minimal and in which the patients respond to specific antithyroid therapy. Within the past two years two patients have been studied by us, both of whom suffered from long standing congestive failure with auricular fibrillation. It was impossible to obtain satisfactory measurements of the basal metabolic rates in these patients. Analyses for PBI were made and the values in the sera of both patients were found to be elevated above 10γ per 100 ml. Cautious administration of propylthiouracil together with cardiac medication was attended by marked improvement in both cases and with the resumption of normal sinus rhythm in one of them.

In a series of 17 patients with hypertensive cardio-vascular disease recently studied by us, the mean value for serum PBI was 6.2γ per 100 ml. This group included one high value of 10.5γ per 100 ml. One patient, not included in the series, was recently studied who suffered from hyperthyroidism accompanied by severe hypertensive disease. In this patient the concentration of PBI in the serum was 31γ per 100 ml. The presence of severe hypertension tended to minimize the degree of thyrotoxicosis. The measurement of PBI was helpful in assaying increased thyroid activity in this patient.

Protein bound iodine concentrations undergo physiological elevations in pregnancy and infancy. A slight physiological decrease in the concentration of PBI is observed in senescence, especially in the male. The effect of stress, environmental temperature and menstruation upon the levels of serum PBI is questionable.

Artefactitious elevations in the levels of PBI are observed following the administration of large doses of inorganic iodide and for variable times following the use of organic iodine-containing compounds, especially those used for the roentgenologic visualization of internal structures. A sharp decrease in PBI values is observed for 24 hours following the administration of mercurial diuretics.

Abstract 7

Untoward Reactions Associated with Apresoline Therapy. M. August Lindauer, M.D., and Joseph H. Hafkenschiel, M.D.

One-hundred and seventy-five patients with essential hypertension have been treated with Hydralazine orally since March 1950. Of these 175 cases, 13 have developed symptoms of rheumatoid arthritis (mild in 9 cases and more severe in 4) with one developing definite lupus erythematosus disseminatus.

Using the symptoms, signs and laboratory data of lupus erythematosus disseminatus as a guide, we have studied these 13 cases and also 20 control cases on Hydralazine for 1–3 years without symptoms. We have attempted to show: 1) that the clinical entities discussed are probably due to drug sensitization reactions; 2) that if looked for, these entities may be noted before the occurrence of serious sequellae and that the situation will revert to normal if the medication is stopped; 3) that the earliest symptom noted by the patient is arthralgia; 4) that these sequellae are not a contraindication to Hydralazine therapy in essential hypertension, but that a consideration of the risks involved and the therapeutic benefit to be obtained is imperative in each patient.

Abstract 8

Allergy to Foods Containing Sulfur-amino Acids, Especially Methionine: Case Report and Clinical Study. Louis Tuft, M.D., L.N. Ettelson, M.D., and Herbert Schwartz, B.S.

A clinical study was carried out upon a 27-year-old atopic male chemist with recurrent urticaria and nasal and cerebral symptoms of allergy. The latter have been attributed since childhood to "sinusitis" but despite negative intracutaneous skin reactions, were proven by diet trial to be due to allergy to certain foods, including egg, garlic and molded cheeses. Thus on repeated occasions ingestion of egg would be followed by nasal and cerebral symptoms lasting varying lengths of time according to the amount eaten. Since the latter was high in content of sulfur-containing amino acids, notably methionine and cystine, and because repeated and deliberate inhalation of H_2S fumes seemed to induce similar reaction, the possibility of an allergy to these amino acids was suggested. Since such laboratory procedures as leukopenic index, oral passive transfer and Coca pulse method were of little value in verifying such a possibility, ingestion experiments were carried out first with methionine and later with empty capsules as controls. These experiments were done first with the knowledge of the patient and later as a blind study so as to eliminate possible prejudice. In the latter case, the patient was given unknown capsules containing methionine, cystine and talc. In both instances, we were able to show repeatedly that ingestion of methionine was followed by the same symptoms which the patient had following the ingestion of egg, whereas cystine produced only slight symptoms and talc none at all. Demonstration of the existence of allergy to protein split-products (in this case amino acids) helps to explain some instances of food allergy with a clinical history but negative skin test reactions.

Abstract 9

A Cool Box to Measure Blood Flow in Peripheral Arterial Disease. Raymond Penneys, M.D.

In patients with peripheral arterial disease, the capacity for blood flow in the extremity can be measured by the reflex vasodilatation test. In this procedure blood flow is obtained by comparing the skin temperature of the limb with the temperature of the surrounding air. The air must be cool (approximately 20° centigrade) in order that the skin temperature–air temperature relationship be a valid measurement of blood flow. In the past, this required that the patient be placed in a thermo-regulated cool room.

In the proposed method, a thermo-regulated cool box is used instead of a thermo-regulated cool room. The extremity in which blood flow measurements is made rests in the box; the patient's body remains in an ordinary room, with uncontrolled air temperature.

Reflex vasodilatation tests were done on a group of subjects (six patients with peripheral arterial disease and three normal subjects) by each of the two methods, and the results compared. There was good agreement between the two methods.

It appears, therefore, that a thermo-regulated cool box may be used, instead of a thermo-regulated cool room, in carrying out the reflex vasodilatation test.

Abstract 10

Cases Returning to Former Occupations Following Myocardial Infarction. William D. Stroud, M.D.

The cardiac histories of seven patients were discussed: 1) a fireman, certified as able, at age 36 (1953), to carry on his duties, three and a half years after evidence of myocardial infarction; 2) a housewife, delivered (1942) by cesarian section of a 6¾ pound boy twenty months after an acute myocardial infarct at age 35; 3) a broker who, after a posterior myocardial infarct at age 37 (1942), worked full time until the day of his death (1952); 4) a patient who carried on work and athletic activities for fourteen years after a coronary thrombosis with myocardial infarction at age 40 (1935); 5) an industrialist who died, apparently from a third myocardial infarct, at age 87 (1943), seventeen years after an initial posterior coronary thrombosis with myocardial infarction, and five years after retirement; 6) a physician, now 74, with cardiac history dating back twenty-five years; 7) a physician who died in his 72d year (1925), seventeen years after his first coronary thrombosis; at 70, he was still leading a fairly active life, playing golf until three years before his death.

List of College Lectures, 1953

7 January 1953

Bauer, Walter. The Evaluation of the Adaptation Concept in Relation to the Connective Tissue Diseases. (Benjamin Musser Lecture IV; *Transactions & Studies*, August, 1953)

4 February 1953

Reimann, Stanley P. A Report on Microscopic Progress in the Chemotherapy of Cancer. (Nathan Lewis Hatfield Lecture XXXVII; *Transactions & Studies*, June, 1953)

4 March 1953

Bard, Philip. Cerebral Mechanisms Involved in the Angry and Aggressive Behavior of Animals. (S. Weir Mitchell Oration XIII; not made available for publication)

1 April 1953

Spink, Wesley W. Epidemiologic and Clinical Studies on Brucellosis, 1937–1952. (James M. Anders Lecture XXIX; *Transactions & Studies*, August, 1953)

*13 May 1953**

Geckeler, George D., *Moderator*. A Symposium on Cardiovascular Diseases. *Speakers:* O. Henry Janton, Lowell L. Lane, Daniel Mason, William Likoff, Franklin C. Massey. (Joint meeting with the Philadelphia County Medical Society)

7 October 1953

Glover, Robert P. The Present Status of Intracardiac Surgery for Mitral and Aortic Stenosis. (Thomas Dent Mütter Lecture LXVI; *Transactions & Studies*, February, 1954)

*4 November 1953**

Moore, Francis D. Isotope Dilution: A Theory, a Method, a Pathway to New Horizons. (Alvarenga Prize Lecture XIII; *Transactions & Studies*, February, 1954)

2 December 1953

Jefferson, Sir Geoffery. Reflections on Pituitary Infantilism. (James M. Anders Lecture XXX; to be published in a later issue of the *Transactions & Studies*)

* *Joint meeting with the Philadelphia County Medical Society.*

Officers, Committees, Sections, and Administrative Staff of the College

1954

President

Richard A. Kern

Vice-President

Lewis C. Scheffey

Secretary

Leandro M. Tocantins

Treasurer

Francis C. Grant

Censors

John H. Gibbon
Edward B. Krumbhaar
O. H. Perry Pepper
J. Parsons Schaeffer

Honorary Librarian

William Egbert Robertson

Ex-Presidential Councillor

T. Grier Miller

Elected Councillors

To serve until January, 1955
William L. Martin
Francis C. Wood

To serve until January, 1956
W. Emory Burnett
David A. Cooper

To serve until January, 1957
John H. Gibbon, Jr.
Burgess L. Gordon

Council

The forenamed and the chairmen of the Standing Committees*

ELECTIVE STANDING COMMITTEES

Library

Jonathan E. Rhoads, *ch'n*
Burton Chance
John F. Huber
O. Henry Janton
J. Earl Thomas

Hall

Joseph B. VanderVeer, *ch'n*
Catharine Macfarlane
Harry Shay
Paul C. Swenson
Harold A. Zintel

Müller Museum and College Collections

R. Philip Custer, *ch'n*
Theodore F. Bach
Peter A. Herbut

Publication

Lawrence S. Carey, *ch'n*
Francis D. W. Lukens
H. Earle Twining

* The President is a member *ex officio* of all Standing Committees.

APPOINTIVE STANDING COMMITTEES

Finance

Arthur M. Dannenberg, *ch'n*
Charles L. Brown
Glen G. Gibson
The Treasurer, *ex officio*

Entertainments

Barton R. Young, *ch'n*
Harold G. Scheie
Morris W. Stroud, 3rd

Scientific Business

Henry L. Bockus, *ch'n*
Kenneth E. Appel
R. Philip Custer
Garfield G. Duncan
O. Spurgeon English
Samuel B. Hadden
Malcolm W. Miller
Jesse T. Nicholson
Donald M. Pillsbury
The Secretary, *ex officio*

Public Health, Preventive Medicine and Public Relations

Samuel B. Hadden, *ch'n*
Harrison F. Flippen
Walter P. Havens, Jr.
John P. Hubbard
Norman R. Ingraham, Jr.

PRIZE COMMITTEES AND TRUSTEES

Alvarenga Prize and Lectureship

O. Spurgeon English, *ch'n*
Robert A. Kimbrough, Jr.
Karl E. Paschkis
William C. Stadie
Joseph B. VanderVeer

Weir Mitchell Oration

Kenneth E. Appel, *ch'n*
John V. Blady
Joseph Hughes
Eugene P. Pendergrass
Joseph Stokes, Jr.

Trustee under the Will of Thomas Skelton Harrison

J. Parsons Schaeffer

Honorary Director of the Department of Medical Arts

Samuel B. Sturgis

Nathan Lewis Hatfield Prize and Lectureship

Jesse T. Nicholson, *ch'n*
Henry P. Royster
H. Curtis Wood, Jr.

Mary Scott Newbold Lectures

Malcolm W. Miller, *ch'n*
John H. Gibbon, Jr.
J. Robert Willson
The President and the Chairman of the Committee on Scientific Business, *ex officiis*

Trustees of Nathan Lewis Hatfield Prize and Lectureship

William D. Stroud
J. Montgomery Deaver
Thomas Fitz-Hugh, Jr.

Honorary Legal Counsel

Eric A. McCouch

OFFICERS OF THE SECTIONS

General Medicine

John Lansbury, *ch'n*
Charles M. Thompson, *clerk*
Executive Committee: William A. Jeffers, William G. Leaman, Jr., Leandro M. Tocantins

Medical History

Samuel X Radbill, *ch'n*
Nicholas Padis, *clerk*
Executive Committee: Maurice S. Jacobs, Herbert T. Kelly, William G. Leaman, Jr.

Ophthalmology

Edmund B. Spaeth, *ch'n*
William E. Krewson, 3rd, *clerk*
Executive Committee: Perce DeLong, Wilfred E. Fry, George F. J. Kelly

Otolaryngology

Benjamin H. Shuster, *ch'n*
Philip A. Marden, *clerk*
Executive Committee: Louis H. Clerf, Robert J. Hunter, M. Valentine Miller

Public Health, Preventive and Industrial Medicine

Katharine R. Boucot, *ch'n*
Robert V. Cohen, *clerk*
Executive Committee: David A. Cooper, Alfred C. LaBoccetta, Pascal F. Lucchesi

---

ADMINISTRATIVE STAFF OF THE COLLEGE

Librarian
Elliott H. Morse

Curator of Library Historical Collections, and Editor
W. B. McDaniel, 2d

Curator of the Mütter Museum and Custodian of the College Collections
Ella N. Wade

Clerk of the College
Olga E. Lang

Assistant Clerk
Dolores Magasich

Superintendent
George S. Allen

Fellows

December 31, 1953

ELECTED

1952. Abelson, Neva Martin, 32 Woodale Rd.
1948. Adelizzi, Richard A., 1723 S. Broad St.
1926. Adler, Francis Heed, 313 S. 17th St.
1949. Aegerter, Ernest E., 3400 N. Broad St.
1953. Agerty, Horst A., 1111 N. 63rd St. (31)
1914. Aiken, Thomas G., Berwyn, Pa.
1936. Alexander, Fay Knight, Germantown Professional Bldg., Greene and Coulter Sts.
1947. Allbritten, Frank F., Jr., 1025 Walnut St.
1932. Allen, Frederick H., 1711 Fitzwater St.
1953. Allman, David B., 104 St. Charles Pl., Atlantic City, N. J.
1935. Alpers, Bernard J., 111 North 49th St.
1930. Appel, Kenneth E., 111 N. 49th St.
1905. Appelman, Leighton Francis, 308 S. 16th St.
1935. Armitage, George L., 400 E. 13th St., Chester, Pa.
1922. Arnett, John H., 2116 Pine St.
1942. Aronson, Joseph D., Henry Phipps Institute, 7th and Lombard Sts.
1952. Ash, Rachel, 5636 Pine St. (43)
1920. †Astley, G. Mason, 812 N. 63rd St.
1952. Aston, Melville J., 2507 S. 21st St.
1944. Atkins, Joseph P., 1201 Knox Rd., Wynnewood, Pa.
1935. Atlee, John L., Jr., 37 E. Orange St., Lancaster, Pa.
1952. Atlee, William A., 37 E. Orange St., Lancaster, Pa.
1935. Bach, Theodore F., 1900 Rittenhouse Sq.
1942. Bachman, Carl, Univ. of Pa. Hospital.
1937. Bacon, Emily P., 1930 Chestnut St.
1952. Baier, Howard N., 3401 N. Broad St.
1952. Baker, Howard W., 3401 N. Broad St.
1946. Baker, Walter W., 255 S. 17th St.
1940. Barba, Philip S., 5919 Greene St.
1943. Barden, Robert P., 8835 Germantown Ave.
1911. Barnard, Everett P., 1820 Rittenhouse Sq.
1939. Barnshaw, Harold D., 406 Cooper St., Camden, N. J.
1939. Bartle, Harvey, Jr., 133 S. 36th St.
1931. Bates, William, 2029 Pine St.
1932. Batson, Oscar V., 3502 Hamilton St.
1921. Bauer, Edward L., 5501 Greene St. (44)
1933. Bauer, John T., 312 E. Second St., Moorestown, N. J.
1939. Baumann, Frieda, 1930 Chestnut St.
1908. Beardsley, E. J. G., 1919 Spruce St.
1930. Beardwood, Joseph T., Jr., 2031 Locust St.
1952. Bedrossian, E. Howard, 2027 Spruce St.
1949. Beecham, Clayton T., Greene & Coulter Sts.
1935. Beerman, Herman, 2422 Pine St.
1942. Behrend, Albert, 255 S. 17th St.

† Died while this list was in press.

1945. Behrend, Bernard, 5910 Greene St.
1934. Behrend, Moses, 255 S. 17th St.
1949. Beizer, Lawrence H., 255 S. 17th St.
1930. Belk, William Parks, 433 Owen Rd., Wynnewood, Pa.
1936. Bell, Benjamin Tertius, Abington Medical Bldg., Keith & York Rds., Abington, Pa.
1947. Bellet, Samuel, 2021 Spruce St.
1952. Bennett, George A., 1025 Walnut St.
1943. Berk, J. Edward, 711 64th Ave.
1941. Bernstein, Mitchell, 7609 Mountain Ave. (17)
1951. Bernstine, J. Bernard, 255 S. 17th St.
1937. Bertolet, J. Allen, 4024 Timber Lane.
1934. Biddle, Sydney Geoffrey, 255 S. 17th St.
1918. Billings, Arthur E., 2020 Spruce St.
1952. Bird, Gustavus C., Jr., 3401 N. Broad St.
1949. Bishop, Edward H., 255 S. 17th St.
1933. Bishop, Paul A., Pennsylvania Hospital.
1944. Blady, John V., 340 Fishers Rd., Bryn Mawr, Pa.
1952. Blake, Paul O., 273 N. Lansdowne Ave., Lansdowne, Pa.
1951. Blank, Harvey, c/o E. R. Squibb & Sons, 745 Fifth Ave., New York 22, N. Y.
1917. Block, Frank B., 305 Tabor Medical Bldg., York & Tabor Rds.
1949. Blumstein, George I., 2039 Delancey St.
1929. Bockus, Henry L., 250 S. 18th St.
1928. Boles, Russell S., Rittenhouse Plaza, 1901 Walnut St.
1923. Bond, Earl D., 111 N. 49th St.
1911. Bonney, Charles W., 255 S. 17th St.
1948. Bookhammer, Robert S., 209 Rittenhouse Claridge. (3)
1931. Bortz, Edward Le Roy, 2021 W. Girard Ave.
1921. Borzell, Francis Frank, 4940 Penn St.
1936. Bostwick, Delazon Swift, 106 Linwood Ave., Ardmore, Pa.
1928. Bothe, Albert E., 255 S. 17th St.
1928. Bothe, Frederick A., 255 S. 17th St.
1951. Boucot, Katharine R., 229 W. Upsal St.
1947. Bourland, Henry S., 2219 Garret Rd., Drexel Hill, Pa.
1923. Bower, John O., 2008 Walnut St.
1942. Bowie, Morris A., Bryn Mawr Medical Bldg., Bryn Mawr, Pa.
1907. Bradley, William Nathaniel, 1725 Pine St.
1942. Branen, William, Whitby & Cypress Ave., Yeadon, Pa.
1921. Bransfield, John W., 2101 Spruce St.
1948. Braun, William, 406 Cooper St., Camden, N. J.
1953. Brav, Solomon S., 5575 N. Park Ave. (41)
1953. Breckenridge, Robert L., Jefferson Hospital. (7)
1951. Brinton, S. Jervis, Fishers Road, Bryn Mawr, Pa.
1946. Briscoe, Clarence Conway, 811 Spruce St. (7)
1953. Brobeck, John R., Univ. of Pa. School of Medicine. (4)
1952. Brody, Morris W., 1930 Chestnut St.
1948. Brogan, Edmund J., Thomas Wynne Apartment, Wynnewood, Pa.
1917. Bromer, Ralph S., 318 Milbank Road, Bryn Mawr, Pa.
1953. Brooke, John A., 1431 Spruce St. (2)
1936. Brown, Charles L., 1030 Indian Creek Rd.
1936. Brown, Clark E., Lankenau Hospital.
1932. Brown, Claude P., 1930 Chestnut St.
1919. Brown, Henry P., Jr., Willow Grove & Cherokee Avenues.

1939. Brust, Raymond W., 4710 Chester Ave.
1953. Bucher, Robert M., 3401 N. Broad St. (40)
1952. Bumgardner, Heath D., 3701 N. Broad St.
1953. Burbidge, J. Raymond, 163 Nassau St., Princeton, N. J.
1940. Burnett, W. Emory, 3401 N. Broad St.
1941. Butler, Miriam, 1930 Chestnut St.
1906. Butler, Ralph, 47th & Pine Sts.
1907. Cadwalader, Williams B., 133 S. 36th St.
1928. Campbell, Edward H., 133 S. 36th St.
1952. Campbell, Edward W., 1318 Medical Arts Bldg.
1944. Campion, Richard J., Penllyn Rd., Springhouse, Ambler, Pa.
1931. Cantarow, Abraham, 1025 Walnut St.
1952. Cardonf, John B., 342 N. 63rd St.
1935. Carey, Lawrence S., 330 S. 9th St.
1931. Cariss, Walter L., 4310 Walnut St.
1930. Carpenter, Chapin, 1930 Chestnut St.
1926. Carpenter, Howard Childs, 1805 Spruce St.
1917. Carson, John B., Newtown Square, Pa.
1937. Castallo, Mario A., 1621 Spruce St.
1943. Castigliano, S. Gordon,853 Mt. Pleasant Rd., Bryn Mawr, Pa.
1949. Caswell, H. Taylor, 3401 N. Broad St.
1950. Chamberlain, Richard H., 3400 Spruce St.
1933. Chamberlain, W. Edward, Temple University Hospital.
1939. Chamberlin, George W., Reading Hospital, Reading, Pa.
1900. Chance, Burton, 317 S. 15th St.
1945. Chance, Burton, Jr., 1726 Spruce St.
1948. Chapman, John P., 71st St. & City Line Ave., Overbrook, Pa.
1950. Chapple, Charles C., Flourtown, Pa.
1939. Charr, Robert Kyun Hyun, 2038 Locust St.
1947. Chouké, Kehar S., P.O. Box 547, Kecoughton, Va.
1945. Cianfrani, Theodore 1930 Chestnut St.
1939. Ciccone, Emmet F., 2021 Murray St.,
1951. Clagett, Augustus H., Jr., 11400 Nemours Bldg., Wilmington, Del.
1929. Clark, Eliot R., 315 S. 41stSt.
1934. Clark, Jefferson Hamer, 11 Maple Ave., Wyncote, Pa.
1951. Clark, John K., University Hospita, 36th & Spruce Sts.
1947. Clark, Thomas Williams, 400 E. Willow Grove Ave.
1947. Classen, Charles H., Cushman Rd. and Lancaster Ave., Rosemont, Pa.
1926. Clerf, Louis H., 1530 Locust St.
1910. Cloud, J. Howard, 111 St. Pauls Road, Ardmore, Pa.
1903. Coates, George Morrison, 1721 Pine St.
1941. Cohen, J. Gershon, 255 S. 17th St.
1951. Cohen, Leon Solis-, 1422 Chestnut St.
1949. Cohen, Louis B., 1320 Arrott St.
1907. Cohen, Myer Solis-, 2110 Spruce St.
1953. Cohen, Robert V., 255 S. 17th St. (3)
1934. Colgan, Robert C., 5882 N. Marshall St.
1934. Collins, Leon Howard, Jr., 133 S. 36th St.
1943. Colonna, Paul C., Univ. of Pa. Hospital.
1949. Conger, Kyril B., 3401 N. Broad St.
1945. Coonel, Pauline, 47 E. Mt. Pleasant Ave.
1930. Cooper, David A., 1520 Spruce St.

1953. Cooper, Donald R., 133 S. 36th St. (4)
1947. Coppolino, John F., 1807 S. Broad St.
1952. Corbit, John D., Jr., 3717 Chestnut St.
1941. Cornelius, Chalmers E., 119 Summit Ave., Jenkintown, Pa.
1911. Cornell, Walter S., Board of Public Education, Parkway and 21st St.
1945. Corrigan, Patrick H., 1720 S. Broad St., Trenton, N. J.
1914. Corson, Edward F., 136 S. 16th St.
1946. Costello, Thomas J., 131 Pennsylvania Avenue, Bryn Mawr, Pa.
1924. Cowan, Alfred, 1930 Chestnut St.
1940. Cowan, Thomas H., 1930 Chestnut St.
1904. Craig, Frank A., The Henry Phipps Institute, 7th and Lombard Sts.
1907. Crampton, George S., 2031 Locust St.
1947. Crane, A. Reynolds, 807 Spruce St.
1937. Crane, Martin P., 2412 N. Broad St.
1920. Creighton, William J., 37 S. 20th St.
1952. Crellin, J. Antrim, 1930 Chestnut St.
1941. Creskoff, Adolph J., 3400 Spruce St.
1920. Cross, George H., 1403 Broom St., Wilmington, Del.
1917. Cross, Sumner H., P.O. Box 126, Jenkintown, Pa.
1921. Crossan, Edward T., 5324 Wayne Ave.
1904. Cruice, John M., 407 S. 22nd St.
1937. Crump, Jean, 1930 Chestnut St.
1937. Curtis, Lawrence, 255 S. 17th St.
1934. Custer, R. Philip, 221 Walnut Ave., Wayne, Pa.
1938. Dannenberg, Arthur M., 235 S. 15th St.
1951. Daugherty, Earl A., 2025 W. Girard Ave.
1953. Davie, John H., 269 S. 19th St. (3)
1947. Davis, C. Nelson, 133 South 36th St.
1936. Davis, David M., 255 S. 17th St.
1951. Davis, J. Wallace, 135 S. 18th St.
1937. Davis, Perk Lee, P.O. Box 701, Paoli, Pa.
1935. Deaver, J. Montgomery, 1830 Delancey Pl.
1947. Dehne, Theodore L., Adams Avenue and Roosevelt Blvd.
1902. Dehoney, Howard, 240 S. 13th St.
1935. Deibert, Irvin Elmer, 538 Cooper St., Camden, N. J.
1948. Deichler, John W., 1930 Chestnut St.
1923. De Long, Perce, 37 S. 20th St.
1952. DeLuca, Charles Q., 255 S. 17th St.
1952. De Orsay, Ralph H., 1241 Lindale Ave., Drexel Hill, Pa.
1951. De Palma, Anthony F., 248 S. 21st St.
1928. Dewees, A. Lovett, Glen Mills, Del. Co., Pa.
1952. Digilio, Victor A., 2200 St. James Place.
1924. Dillon, Edward S., 2028 Delancey Pl.
1953. Dixon, James P., Dept. of Public Health, City Hall Annex. (7)
1920. Doane, Joseph C., 617 W. Hortter St.
1948. Dohan, Francis Curtis, 80 Princeton Road, Cynwyd, Pa.
1946. Donnelly, Andrew J., 33rd and Powelton Ave.
1942. Donnelly, Edward J., 1321 Spruce St.
1933. Donnelly, Joseph C., 6832 Ogontz Ave.
1937. Donnelly, Robert T. M., 255 S. 17th St.
1952. Drayer, Calvin S., 111 N. 49th St.
1949. Dripps, Robert D., 3400 Spruce St.

1935. Duane, William, Jr., Rittenhouse Club, 18th & Walnut Sts.
1944. Dublin, George J., 1930 Chestnut St.
1944. Dugger, John H., 3902 Vaux St.
1935. Duncan, Garfield G., 330 S. 9th St.
1937. Dunn, Charles W., 265 S. 19th St.
1951. Dunne, Francis S., 133 S. 36th St.
1953. Dupler, Donald A., 4028 Walnut St. (4)
1942. Durant, Thomas M., 3401 N. Broad St.
1947. Durkin, John Keenan, 34 W. Montgomery Ave., Ardmore, Pa.
1942. Dyer, W. Wallace, Univ. of Pa. Hospital.
1935. Eads, John T., 2029 Delancey St.
1936. Easby, Mary Hoskins, Woman's Hospital.
1948. Eaton, Francis H., 4007 Chestnut St.
1953. Eberhard, Theodore P., Jefferson Hospital. (7)
1937. Edeiken, Joseph, 2130 Delancey Pl.
1944. Eger, Sherman A., 2029 Delancey St.
1949. Egoville, John W., 720 N. 63rd St.
1944. Ehrich, William E., 540 W. Hortter St.
1930. Eiman, John, Cynwyd, Pa.
1953. Eisenberg, Isadore J., 2117 Spruce St. (3)
1946. Elfman, Louis Kenneth, 6330 Lebanon Avenue.
1949. Elkinton, J. Russell, Oak Lane, Moylan, Pa.
1939. Ellis, Van Mashburn, 1530 Locust St.
1928. Ellison, Richard T., 269 S. 19th St.
1936. Ellson, J. Vernon, 807 Spruce St.
1904. Elmer, Walter G., 1801 Pine St.
1937. Elsom, Kendall A., 133 S. 36th St.
1934. Ely, William C., 3912 Chestnut St.
1932. Engel, Gilson C., 255 S. 17th St.
1945. English, O. Spurgeon, 3401 N. Broad St.
1942. Erb, William H., 133 S. 36th St.
1953. Erf, Lowell A., Jefferson Hospital. (7)
1950. Ersner, Matthew S., 1915 Spruce St.
1948. Everts, Glenn S., 5515 Wissahickon Ave., Apt. D-403.
1946. Farell, David M., 1912 Spruce St.
1903. Farr, Clifford B., Bryn Mawr, Pa.
1945. Farrar, George Elbert, Jr., 528 Scott Rd., Gladwyne, Pa.
1953. Farrell, Harry L., 1930 Chestnut St. (3)
1930. Farrell, John T., Jr., 255 S. 17th St.
1935. Ferguson, Lewis Kraeer, 133 S. 36th St.
1936. Fetter, Ferdinand, 322 S. 21st St.
1945. Fetter, John S., 842 Worrell Rd., Jenkintown, Pa.
1935. Fetter, Theodore R., 255 S. 17th St.
1924. Fewell, Alexander G., 1924 Pine St.
1952. Fields, Harry, 133 S. 36th St.
1943. Finklestein, Arthur, 480 Latch's Lane, Merion, Pa.
1947. First, Arthur, 1714 Spruce St.
1945. Fiske, Frederick A., 1530 Locust St.
1952. Fitts, William T., Jr., 3400 Spruce St.
1928. Fitz-Hugh, Thomas, Jr., 2016 Delancey Pl.
1952. Flexner, Louis B., Univ. of Pa.
1928. Flick, John B., 330 S. 9th St.

1952. Flinn, Lewis B., 503 Delaware Ave., Wilmington, Del.
1939. Flippin, Harrison F., 255 S. 17th St.
1951. Ford, Elbert S. C., 255 S. 17th St.
1941. Fox, C. Calvin, 1806 Spruce St.
1906. Fraley, Frederick, 71st and City Line.
1941. Frazier, William Doane, 419 Gilpin Rd., Narberth, Pa.
1952. Freed, Herbert, 255 S. 17th St.
1953. Fried, Paul H., 1812 Spruce St. (3)
1951. Friedland, Carl K., 133 S. 36th St.
1951. Friedman, Paul Sigmund, 1422 Chestnut St.
1942. Friedman, Reuben, 877 N. 6th St.
1933. Fritch, James Scott, 269 S. 19th St.
1937. Fritz, Herbert H., Pennswood Rd., Bryn Mawr, Pa.
1953. Fruchter, Joseph M., 2104 Pine St. (3)
1940. Fry, Kenneth E., 255 S. 17th St.
1935. Fry, Wilfred Eyles, 1930 Chestnut St.
1937. Furlong, Thomas F., Jr., Times Medical Building, Ardmore, Pa.
1935. Gammon, Geo. D., Univ. of Pa. Hospital.
1951. Garlichs, Richard W., 216 N. Manoa Road, Havertown, Pa.
1931. Garner, Vaughn C., Germantown Professional Building.
1953. Garnet, James D., 330 S. 9th St. (7)
1950. Garvin, Eugene J., 4219 Baltimore Ave.
1953. Geckeler, Edwin O., 269 S. 19th St. (3)
1952. Gefter, William I., 1737 Chestnut St.
1935. Geist, Donald C., 1930 Chestnut St.
1899. Gibbon, John H., Media, Pa.
1934. Gibbon, John H., Jr., 1025 Walnut St.
1939. Gibson, Glen Gregory, 2031 Locust St.
1944. Gifford, Edward S., Jr., 1913 Spruce St.
1920. Gill, A. Bruce, 1930 Chestnut St.
1927. Gilmour, William R., 6616 Woodland Ave. (42)
1952. Gilpin, Sherman F., 255 S. 17th St.
1949. Ginsburg, Isadore W., 3401 N. Broad St.
1931. Giordano, Anthony A. S., 1819 S. Broad St.
1953. Godfrey, Lincoln, 255 S. 17th St. (3)
1945. Goldberg, Samuel J., 1723 Pine St.
1933. Goldburgh, Harold L., 1932 Spruce St.
1935. Goldsmith, N. Ralph, 1351 Tabor Rd.
1949. Gopadze, Illarion I., 1809 Delancey Pl.
1928. Gordon, Burgess L., Woman's Medical College of Pa.
1937. Gordon, William, 5345 Spruce St.
1941. Gouterman, Joseph I., 1930 Chestnut St.
1926. Grant, Francis Clark, Univ. of Pa. Hospital.
1940. Greene, Lloyd B., 136 S. 16th St.
1952. Greening, Roy R., 3400 Spruce St.
1934. Griffith, John Q., Jr., 6 N. Fredericksburg Ave., Margate, N. J.
1945. Griffiths, John E., Mermont Apartments, Bryn Mawr, Pa.
1941. Groff, Robert A., 1930 Chestnut St.
1952. Gross, Elmer R., 1402 Spruce St.
1952. Grotzinger, Paul J., 7163 Georgian Rd.
1952. Grove, D. Dwight, 230 N. Broad St.
1933. Gruber, Charles M., 128 Overhill Rd., Cynwyd, Pa.

1932. Guequierre, Jacques P., Mermont Plaza, Bryn Mawr, Pa.
1945. György, Paul, Univ. of Pa.
1935. Hadden, Samuel B., 250 S. 18th St. (3)
1951. Hafkenschiel, Joseph H., 3600 Spruce St.
1945. Hahn, George A., 255 S. 17th St.
1935. Haines, Harlan F., 134 S. State Rd. Upper Darby, Pa.
1951. Hallett, Joseph W., 1001 Medical Arts Bldg., 16th & Walnut Sts.
1939. Hamblock, Leonard C., 1632 Spruce St.
1938. Hand, John G., 1724 Pine St.
1947. Hanes, William James, 218 E. Beechtree Lane, Wayne, Pa.
1952. Harer, W. Benson, State Rd. & Rogers Ave., Bywood, Pa.
1951. Harkins, Herbert P., 1930 Chestnut St.
1932. Harris, Stanley E., 229 Maple Ave., Delanco, N. J.
1948. Harris, T. N., 2222 N. 53rd St.
1929. Harrison, Francis G., 1900 Spruce St.
1933. Harrison, William John, 135 S. 17th St.
1926. Hartmann, Fred L., 1914 Pine St.
1946. Harvey, Edith E., 406 York Rd., Jenkintown, Pa.
1947. Harvey, Rolfe Marsh, Glenmary & Houston Rds., Radnor, Pa.
1935. Haskell, Benjamin F., 1426 Spruce St.
1946. Hatfield, C. Alexander, 330 S. 9th St.
1947. Havens, Walter Paul, Jr., 300 Cherry Lane, Wynnewood, Pa.
1947. Hawthorne, Herbert Reid, 255 S. 17th St. (3)
1952. Hayllar, Benjamin L., 801 Medical Arts Bldg.
1911. Heed, Charles R., College Ave. & Coopertown Rd., Haverford, Pa.
1946. Hendrickson, Frank O., 37 S. 20th St.
1953. Henny, George C., 3400 N. Broad St. (40)
1944. Herbut, Peter A., Jefferson Medical College Hospital.
1953. Herrick, William C., Jefferson Hospital. (7)
1951. Herrman, Clinton S., 255 S. 17th St.
1944. Hershey, J. Ivan, 935 Bowman Ave., Wynnewood, Pa.
1924. Hewson, William, 1614 Locust St.
1949. Heyl, W. Meredith, 100 W. Coulter St.
1952. Hinkson, DeHaven, 329 N. 40th St.
1924. Hirst, John C., 2d, 500 N. 20th St.
1943. Hitschler, William J., 8840 Germantown Ave.
1944. Hneleski, Ignatius S., 802 S. 48th St.
1943. Hockaday, Agnes, 316 Shadeland Ave., Drexel Hill, Pa.
1939. Hodes, Philip J., Univ. of Pa. Hospital.
1947. Hodges, John H., 1025 Walnut St.
1948. Hoffman, George L., Jr., 133 S. 36th St.
1949. Hollander, Joseph L., 36th & Spruce Sts.
1932. Hollingsworth, I. Pemberton, 411 N. Walnut St., West Chester, Pa.
1951. Hollis, Charles B., 1930 Chestnut St.
1952. Holloway, Edward E., 1739 W. Montgomery Ave.
1949. Hopkins, Henry U., 4526 Osage Ave.
1953. Horan, Charles A., 734 N. 63rd St. (31)
1946. Horan, Gerald W., 5819 Chester Ave.
1950. Horn, Robert C., 57 Berkley Ave., Lansdowne, Pa.
1947. Horwitz, Orville, 133 S. 36th St.
1953. Hostelley, W. Vernon, 1221 Harrison St. (24)
1950. Houlihan, Carl T., 728 S. 60th St.

1944. Housel, Edmund L., 255 S. 17th St.
1928. Houser, Karl Musser, 2035 Delancey Pl.
1938. Howell, John Carnett, 326 S. 19th St.
1948. Howland, Alvin Wilcox, 255 S. 17th St.
1946. Howson, John Yeatts, 316 Lancaster Ave., Wayne, Pa.
1951. Hubbard, John P., University of Penna., School of Medicine.
1947. Huber, John Franklin, Temple University Hospital.
1937. Hughes, Joseph, 111 N. 49th St.
1939. Hughes, P. Boland, 419 Hillbrook Rd., Bryn Mawr, Pa.
1923. Hume, John E., 900 S. 49th St.
1951. Hundley, J. Warren, 3818 Chestnut St.
1946. Hunt, William T., Jr., 1930 Chestnut St.
1921. Hunter, Robert John, Univ. of Pa. Hospital.
1926. Husik, David N., 331 S. 46th St.
1952. Hyman, Harold L., 3401 N. Broad St.
1950. Imbriglia, Joseph E., 329 Shadeland Ave., Drexel Hill, Pa.
1952. Imperiale, C. Charles, 1331 Pine St.
1935. Ingleby, Helen, Jewish Hospital, York & Tabor Rds.
1949. Ingraham, Norman R., Jr., Stenton and Whitemarsh Ave.
1951. Isard, Harold J., Mt. Sinai Hospital, 5th & Reid Sts.
1951. Israel, Harold L., 255 S. 17th St.
1947. Israel, S. Leon, 2116 Spruce St.
1952. Iverson, Preston C., 1930 Chestnut St.
1921. Ivy, Robert H., 1930 Chestnut St.
1953. Jack, H. Wesley, 538 Cooper St., Camden, N. J. (2)
1917. Jackson, Chevalier, 3401 N. Broad St.
1932. Jackson, Chevalier L., Rittenhouse Plaza, 19th & Walnut Sts.
1934. Jacobs, Maurice, 1831 Delancey Place.
1947. Jaeger, Rudolph, Jefferson Hospital.
1952. Janton, O. Henry, 230 N. Broad St.
1941. Jeffers, William A., University of Pa. Hospital.
1928. †John, Rutherford L., 256 S. 21st St.
1942. Johnson, Julian, 406 Conshohocken State Rd., Narberth, Pa.
1938. Johnson, Thomas A., 250 S. 18th St.
1952. Jonas, Karl C., 3401 N. Broad St.
1918. Jonas, Leon, 255 S. 17th St.
1924. Jones, Harold W., 1930 Chestnut St.
1952. Jones, Jr. Ralph, 3400 Spruce St.
1936. Kain, Thomas M., 403 Cooper St., Camden, N. J.
1948. Kaplan, Louis, 2040 Pine St.
1938. Kasper, Kelvin A., 135 S. 18th St.
1945. Katz, G. Henry, 111 N. 49th St.
1941. Kauffman, M. Luther, Medical Arts Bldg., Jenkintown, Pa.
1947. Kay, Calvin Frederick, Univ. of Pa. Hospital.
1947. Keefer, George Pfahler, 3708 Woodland Ave., Drexel Hill, Pa.
1949. Keiserman, Joseph, 5460 Baltimore Ave.
1935. Kelley, George F. J., N. E. Cor. 20th and Chestnut Sts.
1932. Kelly, Herbert T., 1900 Spruce St.
1912. Kelly, Thomas C., 105 School Lane.
1941. Kennedy, Patrick J., 6910 Market St., Upper Darby, Pa.
1947. Kennedy, William Blair, 3400 Spruce St.
1948. Kern, Franklin Moore, 408 E. Wynnewood Rd., Wynnewood, Pa.

1921. Kern, Richard A., Temple University Hospital.
1935. Keyes, Baldwin L., 2031 Locust St.
1930. Kimbrough, Robert A., Jr., 807 Spruce St.
1936. King, Orville C., 330 S. 9th St.
1952. Kirshner, Jacob J., 1930 Chestnut St.
1920. Klauder, Joseph V., 1934 Spruce St.
1920. Klein, Thomas, 250 S. 18th St.
1952. Kleinbart, Morris, 1922 Pine St.
1934. Kline, Oram R., 514 Cooper St., Camden, N. J.
1948. Klingensmith, Paul O., 133 S. 36th St.
1932. Klopp, John W., 731 E. Phil-Ellena St.
1919. Knipe, Norman L., 514 Baird Rd., Merion, Pa.
1908. Knowles, Frank C., 423 Warick Rd., Wynnewood, Pa.
1945. Kobler, H. B., 658 N. 63rd St.
1914. Kolmer, John A., Cynwyd, Pa.
1936. Konzelmann, Frank Williamson, 12 E. Lenox St. Chevy Chase, Md.
1949. Koop, C. Everett, 1740 Bainbridge St.
1952. Kornblueh, Igho H., 1241 W. Lehigh Ave.
1941. Krall, J. Thomas, 1927 Spruce St.
1948. Kramer, David W., 2007 Pine St.
1944. Krauss, Frederick Harold, 16th & Walnut Sts.
1952. Kravitz, Charles H., 1726 Widener Pl.
1949. Kremer, David N., 1918 Pine St.
1949. Kressler, Robert J., 330 S. 9th St.
1941. Krewson, William E., 3rd, 1930 Chestnut St.
1914. Krumbhaar, Edward B., School of Medicine, Univ. of Pa.
1953. Krumperman, LeRoy W., 3401 N. Broad St. (40)
1947. Kuhlenbeck, Hartwig, Woman's Medical College.
1947. La Boccetta, Alfred Charles, 2nd and Luzerne Sts.
1952. Lachman, John W., 3401 N. Broad St.
1949. La Clair, Charles H., Jr., 1021 W. Main St., Norristown, Pa.
1952. Lafferty, Henry D., 37 S. 20th St.
1951. Lame, Edwin L., 51 N. 39th St.
1950. Lamont, Austin, 3400 Spruce St.
1946. Lampe, William T., 4207 Tyson Ave.
1952. Lang, Warren R., 255 S. 17th St.
1933. Langdon, Roy L., 5917 Greene St.
1941. Langner, Paul H., Jr., 1208 Edmonds Ave., Drexel Hill, Pa.
1945. Lansbury, John, 3401 N. Broad St.
1926. Laws, George M., 1907 Spruce St.
1936. Leaman, William G., Jr., Presidential Apts: Adams House B-909.
1950. Learner, Norman, 255 S. 17th St.
1920. Leavitt, Frederic Headley, 1527 Pine St.
1941. Leberman, Paul R., 136 S. 16th St.
1942. Lehman, James A., 255 S. 17th St.
1952. Lehman, J. Stauffer, 230 N. Broad St.
1951. Leivy, Frank E., 1321 Spruce St.
1944. Lell, William A., 203 W. Chestnut Ave.
1935. Lemmon, William T., 133 S. 36th St.
1943. Leopold, Irving H., 1930 Chestnut St.
1920. Leopold, Simon S., 255 S. 17th St.
1944. Lettiere, Anthony J., 425 E. State St., Trenton, N. J.

1933. Levering, J. Walter, Abington Memorial Hospital, Abington, Pa.
1915. Lewis, Fielding O., Providence Road, Media, Pa.
1938. Lewis, James P., 3815 Chestnut St.
1949. Lhamon, William T., Univ. of Pa. Hospital.
1948. Lieber, Marshall M., 1025 Walnut St.
1948. Lieberman, Louis M., 923 Belmont Ave.
1940. Limberger, William A., 301 S. Church St., West Chester, Pa.
1938. Lindauer, M. August, 133 S. 36th St.
1927. Lindsey, Walter H., 810 W. Dauphin St.
1936. Lintgen, Charles, 1930 Chestnut St.
1953. Lipsius, Edward I., 1923 Spruce St. (3)
1945. Lisker, Samuel, 255 S. 17th St. (3)
1944. Livezey, Mary M., 7200 Cresheim Rd.
1936. Llewellyn, Thomas H., 910 N. 63rd St.
1907. Lodholz, Edward, 431 S. 45th St.
1931. Loewenberg, Samuel A., 1905 Spruce St.
1933. Long, Esmond R., Henry Phipps Institute, 7th and Lombard Sts.
1949. Long, Joan Humphrey, 198 Lafayette Ave., Haddonfield, N. J.
1951. Long, Joseph P., 1930 Chestnut St.
1935. Long, William L., 2025 Walnut St.
1931. Longaker, Edwin P., 41 E. Montgomery Ave., Ardmore, Pa.
1951. Lorber, Stanley H., 3400 N. Broad St.
1942. Lownes, John B., 924 Medical Arts Bldg.
1936. Lucchesi, Pascal Francis, 601 E. Gorgas Lane.
1921. Lucké, Balduin H. E., School of Medicine, Univ. of Pa.
1932. Lukens, Francis D. W., Univ. of Pa. Hospital.
1930. Lukens, Robert M., 1308 W. Hunting Park Ave.
1939. Luongo, Romeo A., 2054 Locust St.
1947. Lurie, Max B., Henry Phipps Institute, 7th and Lombard Sts.
1951. Luscombe, Herbert A., 136 S. 16th St.
1952. Lutman, Frank C., 100 W. Coulter St.
1919. Lynch, Frank B., Jr., Germantown Hosp., Penn and Chew Sts.
1950. Lynch, J. Edward, 255 S. 17th St.
1953. Lyons, John W., 255 S. 17th St. (3)
1933. McAndrews, Leo F., Bryn Mawr Medical Bldg., Bryn Mawr, Pa.
1952. McCabe, Edward S., 2025 Walnut St. (3)
1932. McCahey, James F., 1534 Pine St.
1900. McCarthy, Daniel J., 2025 Walnut St.
1936. McCarthy, Patrick A., Central Medical Bldg.
1935. McClenahan, William U., 1 Summit Ave.
1931. McCloskey, Edward, 7 E. Chestnut Ave. (18)
1953. McCloskey, Joseph F., Jefferson Hospital. (7)
1935. McConnell, James W., 20th and Chestnut Sts.
1934. McCouch, Grayson P., Medical School, Univ. of Pa.
1938. McCrea, Lowrain E., 1930 Chestnut St.
1937. McCutcheon, Morton, Cambridge Apts.
1942. McDonald, P. Robb, 1930 Chestnut St.
1953. McDonnell, William V., 1025 Walnut St. (7)
1952. McElroy, Robert C., 133 S. 36th St.
1950. McFadden, William M., 1187 E. Washington Lane.
1949. McGavic, John S., 601 Montgomery Ave., Bryn Mawr, Pa.
1945. McGee, Lemuel Clyde, Hercules Powder Company, Wilmington, Del

1952. McGlade, Thomas H., 719 Cooper St., Camden, N. J.
1937. McGuinness, Aims C., Children's Hospital, 1740 Bainbridge St.
1940. McLaughlin, Edward F., 4116 N. Broad St.
1933. McLaughlin, James S., 330 S. 9th St.
1924. McMillan, Thomas M., 2044 Locust St.
1924. McPhedran, F. Maurice, Germantown Hosp., Penn and Chew Sts.
1943. Macfarlan, Douglas, 1805 Chestnut St.
1932. Macfarlane, Catharine, 136 S. 16th St.
1947. Machella, Thomas E., Univ. of Pa. Hospital.
1950. Mackmull, Gulden, Germantown Professional Building.
1949. MacNeal, Perry Scott, 330 S. 9th St.
1939. Macneill, Norman N., 5807 Chew St.
1951. Mac Neish, W. J., Medical Arts Bldg., 16th & Walnut Sts.
1935. Maeder, LeRoy M. A., 1910 Rittenhouse Sq.
1952. Mahoney, J. Francis, 250 S. 18th St.
1942. Manges, Lewis C., Jr., 319 S. 16th St.
1936. Mann, Bernard, 2019 Pine St.
1953. Marbach, A. Herbert, 255 S. 17th St. (3)
1948. Marden, Philip Ayer, 1912 Spruce St.
1937. Margolies, Alexander, 1351 Tabor Rd.
1950. Mark, George E., 3401 N. Broad St.
1950. Marshall, E. Wayne, Jr., 1520 Spruce St.
1941. Martin, James R., 1025 Walnut St. (7)
1951. Martin, William L., Hahnemann Hospital.
1952. Martucci, Albert A., 1460 E. Cheltenham Ave.
1953. Marx, Halvey E., 4213 Chester Ave. (4)
1953. Massey, Franklin C., 136 S. 16th St. (2)
1939. May, Hans, 255 S. 17th St.
1934. Mecray, Paul M., 405 Cooper St., Camden, N. J.
1952. Mecray, Paul , Jr., 405 Cooper St., Camden, N. J.
1951. Medinger, Frederick G., 255 S. 17th St.
1941. Mendell, Theodore H., 2023 Spruce St.
1951. Mendelssohn, Edwin, 255 S. 17th St.
1949. Menkin, Valy, 3401 N. Broad St.
1943. Meranze, David R., 1031 Lakeside Ave.
1937. Meyer, George Phillip, 410 Haddon Ave., Camden, N. J.
1935. Miller, Ford A., 4016 Chestnut St.
1946. Miller, Franklin R., Jefferson Medical College.
1939. Miller, Malcolm W., 255 S. 17th St.
1939. Miller, Merle M., 6013 Greene St.
1932. Miller, M. Valentine, 114 W. Phil-Ellena St.
1921. Miller, T. Grier, 133 S. 36th St.
1952. Minehart, John R., 4821 Germantown Ave.
1952. Mintz, S. S., 1429 S. 5th St.
1937. Missett, Joseph Vincent, Jr., 2031 Locust St.
1904. Mitchell, Charles Franklin, 2003 Pine St.
1950. Mitchell, John McK., Medical School, Univ. of Pa.
1952. Mitchell, Robert McNair, 330 S. 9th St.
1948. Mogavero, Francesco, 1930 Chestnut St.
1932. Mohler, Roy W., 1806 Spruce St.
1936. Montgomery, Hugh, 119 Glenn Road, Ardmore, Pa.
1936. Montgomery, John B., 1930 Chestnut St.

1932. Montgomery, Thaddeus L., 2031 Locust St.
1951. Moore, Edward J., 204 Meeting House Lane, Merion, Pa.
1935. Moore, John Royal, Beury Bldg., Broad St. and Erie Ave.
1947. Moore, Matthew Thibaud, 1813 Delancey Pl.
1924. Moorhead, Stirling W., 1523 Pine St.
1936. Morgan, David R., Jefferson Medical College.
1893. Morris, Elliston J., 439 Midland Ave., St. Davids, Del. Co., Pa.
1944. Morris, Harold H., Villa Nova, Pa.
1945. Morris, I. Paul, 255 S. 17th St.
1941. Mucklé, Craig Wright, 330 S. 9th St. (7)
1929. Mudd, Stuart, Department of Bacteriology, Medical School, Univ. of Pa.
1949. Mulholland, Stanford W., 20th & Parkway.
1935. Mullen, Carroll Richard, 2025 Locust St.
1934. Mullen, Edward A., 472 Roxborough Ave.
1930. Murphy, Douglas P., Univ. of Pa. Hospital.
1953. Murphy, Edward J., Bryn Mawr Medical Bldg., Bryn Mawr, Pa.
1951. Myers, David, 304 S. 19th St.
1945. Naide, Meyer, 2034 Spruce St.
1951. Naidoff, David, 3500 Tudor St. (36)
1950. Nardone, Anthony A., 912 S. 49th St.
1950. Neefe, John R., 2021 Delancey Pl.
1948. Neese, Paul H., 17 Derwen Road, Cynwyd, Pa.
1936. Nelson, Guy M., 255 S. 17th St.
1943. Nelson, Waldo E., 615 Moreno Rd., Narberth, Pa.
1905. Newcomet, William S., 3501 Baring St.
1938. Newton, Zachariah B., 601 E. Sedgwick St.
1935. Nicholson, Jesse Thompson, Pennsylvania Hospital.
1941. Nisbet, Verner, 254 S. 45th St.
1950. Nixon, Norman, 111 N. 49th St.
1947. Noone, Ernest L., 4501 Cedar Lane, Drexel Hill, Pa.
1905. Norris, Charles C., Darby and Goshen Roads, Bryn Mawr, Pa.
1938. Norris, Robert F., 513 Wynnewood Ave., Wynnewood, Pa.
1947. O'Keefe, John J., 255 South 17th St.
1913. O'Neal, Alexander Hay, St. Davids, Pa.
1949. O'Neill, James F., 140 Roslyn Ave., Glenside, Pa.
1947. Ornsteen, A. M., 2007 Delancey Pl.
1947. Ornston, Darius Gray, 36 Carpenter Lane.
1936. Orr, Theodore E., 1930 Chestnut St.
1913. Outerbridge, George W., 1927 Spruce St.
1915. Owen, Hubley R., 311 S. Juniper St.
1949. Padis, Nicholas, 255 S. 17th St.
1909. Parish, Benjamin Dores, 1927 Spruce St.
1945. Park, Felix Roman, Medical Arts Bldg., Tulsa, Okla.
1940. Parker, Alan P., Bryn Mawr Medical Bldg., Bryn Mawr, Pa.
1948. Parkhurst, Leonard Woods, 330 S. 9th St.
1944. Paschkis, Karl E., Jefferson Medical College.
1952. Paxson, Newlin F., 250 S. 18th St.
1932. Payne, Franklin L., Univ. of Pa. Hospital.
1943. Pearson, Gerald H. J., 111 N. 49th St.
1952. Peck, Roy I., 3400 Spruce St.
1930. Pendergrass, Eugene P., Univ. of Pa. Hospital.
1953. Penneys, Raymond, 2622 Lenape Rd. (31)

1914. Pepper, O. H. Perry, Univ. of Pa. Hospital.
1916. Percival, Milton Fraser, 2332 S. Broad St.
1942. Perkins, William Harvey, 1025 Walnut St.
1946. Perloff, William Harry, 1930 Chestnut St.
1951. Perri, Angelo M., 814 Federal St.
1953. Persky, Abram H., 1737 Chestnut St. (3)
1940. Pessel, Johannes F., 224 West State St., Trenton, N. J.
1952. Peters, Michael, 262 W. Broad St., Telford, Pa.
1940. Pettit, Horace, Times Medical Bldg., Ardmore, Pa.
1949. Pettit, Mary DeWitt, 1930 Spruce St.
1905. Pfahler, George E., 1930 Chestnut St.
1915. Pfeiffer, Damon B., Meadowbrook, Pa.
1946. Pfeiffer, Mildred C. J., 358 Valley Rd., Merion, Pa.
1935. Phillips, Arthur W., 3904 Walnut St.
1911. Piersol, George Morris, Univ. of Pa. Hospital.
1948. Pierson, Daniel B., Jr., 1830 Delancey St.
1933. Pillsbury, Donald M., Univ. of Pa. Hospital.
1950. Pincus, Irwin J., 269 S. 19th St.
1951. Poinsard, Paul J., 2031 Locust St.
1937. Polk, David Stewart, Rosemont, Pa.
1953. Porreca, George A., 1912 Spruce St. (3)
1932. Porter, Roland De Lance, Abington, Pa.
1953. Posey, William C., Jr., 600 Suburban Square Bldg., Ardmore, Pa.
1951. Post, Joseph W., 1930 Chestnut St.
1951. Pote, Harry H., 4032 Walnut St.
1949. Pratt, Gerald E., 3009 Frankford Ave.
1951. Pressman, Robert S., 269 S. 19th St.
1947. Prickett, John A., Warrington, Bucks County, Pa.
1931. Pryor, Charles Allen, 255 S. 17th St.
1952. Pugh, James E., 614 Church Lane, Yeadon, Pa.
1947. Putney, Floyd Johnson, 255 S. 17th St. (3)
1943. Radbill, Samuel X., 7043 Elmwood Ave.
1953. Radbill, Sidney G., 37 S. 20th St. (3)
1945. Rakoff, Abraham Edward, 269 S. 19th St.
1953. Ralston, Edgar L., 3400 Spruce St. (4)
1931. Ramsey, Frank M., 620 E. Willow Grove Ave.
1953. Ranieri, Tito A., Bryn Mawr Medical Bldg., Bryn Mawr, Pa.
1941. Rankin, Charles A., Ludlow & Heather Rd., Upper Darby, Pa.
1946. Rapoport, Milton, Children's Hospital, 1740 Bainbridge St.
1951. Rathmell, Thomas K., 446 Bellevue Ave., Trenton, N. J.
1926. Ravdin, I. S., Univ. of Pa. Hospital.
1928. Reese, Warren S., 2118 Locust St.
1925. Reeves, Rufus S., Presidential Apts., A-910.
1920. Rehfuss, Martin E., 131 St. George's Rd., Ardmore, Pa.
1921. Reiff, E. Paul, 1927 Spruce St.
1919. Reimann, Stanley P., 703 W. Phil-Ellena St.
1951. Rentschler, Laurence B., 5800 Ridge Ave.
1945. Rhoads, Jonathan E., Univ. of Pa. Hospital.
1936. Richards, James L., Bryn Mawr Medical Bldg., Bryn Mawr, Pa.
1951. Richardson, Fred Mac D., 160 Carpenter Lane.
1919. Richardson, Russell, 605 Suburban Sq., Ardmore, Pa.
1951. Riegel, Donald, 5110 Chester Ave.

1942. Riggs, Helena E., Philadelphia General Hospital.
1936. Ritter, Joseph A., 2405 N. 54th St.
1932. Robbins, Frederick R., 317 Milbank Rd., Bryn Mawr, Pa.
1952. Robbins, Robert, 3401 N. Broad St.
1939. Roberts, Ella, 133 S. 36th St.
1899. Roberts, Walter, 335 S. Camac St. (7)
1932. Robertson, Harold F., 2118 Pine St.
1903. Robertson, William Egbert, 2118 Pine St.
1938. Roche, Philip Q., 255 S. 17th St.
1912. Rodman, John Stewart, American Board of Surgery, 255 S. 15th St.
1947. Rogers, Arthur Merriam, Univ. of Pa. Hosp. (4)
1934. Rogers, Harry L., 255 S. 17th St.
1951. Ronis, Bernard J., 2106 Spruce St.
1948. Roscoe, Constantine R., 7226 Castor Ave.
1928. Rose, Edward, 426 Owen Rd., Wynnewood, Pa.
1936. Rose, Elizabeth Kirk, 426 Owen Rd., Wynnewood, Pa.
1952. Rose, S. Brandt, Chestnut Hill Hospital.
1946. Rosemond, George Parrott, Temple University, Broad & Ontario Sts.
1948. Rothman, Maurice M., 1727 Spruce St.
1932. Rothrock, Harry A., West Chester, Pa.
1936. †Rothschild, Norman, 245 S. 16th St.
1951. Rouse, Jr., George P., 2031 Locust St.
1952. Roxby, Bruce S., 5501 Greene St.
1937. Roxby, John B., 113 Yale Ave., Swarthmore, Pa.
1949. Royster, Henry P., 3400 Spruce St.
1941. Royster, Jr., Hubert A., The Mermont, Bryn Mawr, Pa.
1952. Rubin, I. Edward, 255 S. 17th St. (3)
1933. Rudolphy, Jay Besson, 230 S. 21st St.
1946. Rupp, Charles, 133 S. 36th St.
1947. Rush, Alexander, 330 South 9th St.
1945. Rynes, Samuel E., 334 S. 21st St.
1952. Sain, Fletcher D., Abington Memorial Hospital, Abington, Pa.
1952. Salner, Nathan P., 6812 Castor Ave. (24)
1952. Saltzman, Maurice, 1923 Spruce St.
1944. Sampson, David Alan, 726 Braeburn Lane, Penn Valley, Narberth, Pa.
1936. Sands, Joseph Evans, Rosemont, Pa.
1950. Sarner, Joseph B., 269 S. 19th St. (3)
1949. Saul, Leon J., Highland Ave., Media, Pa.
1908. Sautter, Albert C., Germantown Professional Bldg.
1947. Sayen, John J., 506 Montgomery Ave., Haverford, Pa.
1953. Scanlan, Robert L., Germantown Hospital. (44)
1948. Scarano, Joseph Albert, 1432 S. Broad St.
1920. Scarlett, Hunter W., 825 Montgomery Ave., Bryn Mawr, Pa.
1917. Schaeffer, J. Parsons, Daniel Baugh Institute, 307 S. 11th St.
1929. Scheffey, Lewis C., 255 S. 17th St.
1942. Scheie, Harold G., 313 S. 17th St.
1929. Schenck, Harry P., 1235 Wyngate Rd., Wynnewood, Pa.
1945. Schlezinger, Nathan S., 255 S. 17th St.
1917. Schnabel, Truman G., 1704 Pine St.
1917. Schoff, Charles H., Media, Pa.
1952. Schulz, Norbert J., 1901 Walnut St.
1921. Schumann, Edward A., 8815 Germantown Ave. (18)

1950. Schumann, Francis N., 8811 Germantown Ave.
1948. Schwarz, Gabriel A., 255 S. 17th St.
1930. Scott, John Porter, Children's Hospital, 1740 Bainbridge St.
1950. Scott, Michael, 255 S. 17th St.
1940. Scott, T. F. McNair, Children's Hospital, 1740 Bainbridge St.
1952. Seifer, Arthur F., 3401 N. Broad St.
1951. Seitchik, Joseph N., 1417 Race St., Hahnemann Medical College Annex.
1952. Semisch, Charles W., III, 5329 Rising Sun Ave.
1951. Shaffer, Bertram, 1825 Pine St.
1924. Shallow, Thomas A., 1611 Spruce St.
1950. Sharp, Reuben L., 719 Cooper St., Camden, N. J.
1928. Sharpless, Frederick C., Beach Haven, N. J.
1948. Shay, Harry, 3400 N. Broad St.
1946. Shepherd, Samuel Garfield, 2039 Pine St.
1932. Sheridan, Joyce T., 412 W. Durham St.
1936. Shipman, James Shelby, 255 S. 17th St.
1935. Shoemaker, Robert, 3rd, 68 Byberry Rd., Hatboro, Pa.
1946. Shoup, George Daniel, 121 W. Walnut Lane. (44)
1952. Shuman, Charles R., 3401 N. Broad St.
1936. Shuster, Benjamin H., 1824 Pine St.
1949. Sidlick, David M., 255 S. 17th St.
1941. Silcox, Louis E., 255 S. 17th St.
1952. Skromak, Stanley J., 5108 Torresdale Ave.
1929. Smith, Austin T., 1830 Spruce St.
1933. Smith, Lauren Howe, 111 N. 49th St.
1952. Smith, Richard T., 330 S. 9th St.
1927. Smyth, Calvin Mason, Abington Memorial Hospital, Abington, Pa.
1951. Snape, William J., 573 Stevens St., Camden, N. J.
1938. Snodgrass, L. E., 709 Walnut St. (6)
1953. Snyder, G. Gordon, Bryn Mawr Medical Bldg., Bryn Mawr, Pa.
1935. Sokoloff, Martin J., 255 S. 17th St.
1940. Soloff, Louis A., 255 S. 17th St.
1950. Somerville, William J., 2022 Locust St.
1935. Sommer, George N. J., 120 W. State St., Trenton, N. J.
1944. Sommer, George N. J., Jr., 120 W. State St., Trenton, N. J.
1952. Sones, Maurice, Mt. Airy Medical Bldg.
1951. Sonneborn, Duane G., 1200 W. Erie Ave.
1928. Spaeth, Edmund B., 1930 Chestnut St.
1937. Spangler, John Luther, Devon, Pa.
1935. Spiegel, Ernest, 6807 Lawnton Ave., Oak Lane.
1944. Stadie, William C., University Hospital.
1927. Starr, Isaac, 505 Cresheim Valley Rd.
1952. Stauffer, Herbert M., 3401 N. Broad St.
1952. Stayman, Joseph W., Jr., Germantown Hospital.
1945. Stecher, H. Armin, 1510 Darby Rd., Havertown, Pa.
1953. Steele, Brandt F., 1640 Pine St. (3)
1952. Steele, Eleanor A., 1640 Pine St.
1952. Steiger, William A., 3432 N. Broad St.
1946. Stein, Irvin, 1936 Spruce St.
1953. Stein, Raymond O., 1936 Spruce St. (3)
1936. Steinfield, Edward, N. E. Cor. 18th and Chestnut Sts.
1942. Stengel, Alfred, Jr., 160 Hodge Rd., Princeton, N. J.

1951. Sterling, Julian A., 255 S. 17th St.
1948. Stevens, Lloyd W., 133 S. 36th St.
1941. Stewart, Winifred B., 1930 Spruce St.
1949. Stockwell, Eunice L., 2018 Pine St.
1925. Stokes, John H., 4228 Spruce St.
1928. Stokes, Joseph, Jr., Children's Hospital, 1740 Bainbridge St.
1943. Stokes, S. Emlen, 129 Chester Ave., Moorestown, N. J.
1952. Stoner, Emery K., 222 E. Mt. Pleasant Ave.
1953. Strawbridge, Rendall R., 269 S. 19th St. (3)
1923. Strecker, Edward A., 111 N. 49th St.
1953. Stroud, Morris W., 3rd, Dept. of Pharmacology, Univ. of Pa. (4)
1923. Stroud, William Daniel, 1011 Clinton St.
1937. Strumia, Max M., Penn Valley, Narberth, Pa.
1937. Sturgis, Margaret C., 349 Wistar Rd., Wynnewood, Pa.
1927. Sturgis, Samuel Booth, 349 Wistar Rd., Wynnewood, Pa.
1934. Summey, Thomas J., 330 S. 9th St.
1930. Sunderman, F. William, 6627 Greene St.
1936. Surver, James Miller, 1020 Clinton St.
1928. Swartley, William B., 6002 Greene St.
1944. Swenson, Paul C., Jefferson Hospital.
1948. Tait, Edwin Forbes, 1324 Main St., Norristown, Pa.
1943. Tassman, Isaac S., 136 S. 16th St.
1946. Tauber, Robert, 2019 Walnut St.
1952. Taylor, Ann Gray, 6364 Germantown Ave.
1931. Taylor, Norman H., 100 W. Evergreen Ave.
1952. Teague, Russell E., Harrisburg, Pa.
1951. Theodos, Peter A., 1930 Chestnut St.
1946. Thomas, Carmen C., 1930 Chestnut St.
1928. Thomas, J. Earl, Drexel Hill, Pa.
1952. Thompson, Charles M., 255 S. 17th St.
1927. Thorington, J. Monroe, 2031 Chestnut St.
1936. Thornton, Mary Bickings-, 2703 West Somerset St.
1936. Thorp, Francis Quicksall, 4900 Penn St.
1936. Thudium, William J., 136 S. 16th St.
1935. Tocantins, Leandro Maués, 1025 Walnut St.
1945. Toland, Joseph J., Jr., 1241 W. Lehigh Ave.
1935. Toland, Owen J., Episcopal Hospital, Front and Lehigh Ave.
1952. Tondreau, Roderick L., 227 Crosshill Rd., Penn Wynne, Pa.
1952. Tompkins, Winslow T., 330 S. 9th St.
1953. Topping, Norman H., 3446 Walnut St. (4)
1949. Tornay, Anthony S., 37 S. 20th St.
1945. Tourish, William J., 115 Childs Ave., Drexel Hill, Pa.
1949. Town, Arno E., 255 S. 17th St.
1936. Towson, Charles Emory, Germantown Professional Bldg.
1908. Tracy, Stephen E., Old Arch Rd., Norristown, Pa.
1953. Tropea, Frank, Jr., 269 S. 19th St. (3)
1947. Trueman, Robert H., 1930 Chestnut St.
1926. Tucker, Gabriel, 250 S. 18th St.
1938. Tuft, Louis, 1530 Locust St.
1933. Tumen, Henry J., 1900 Rittenhouse Sq.
1938. Turman, Christopher M., Wyncote, Pa.
1923. Turner, Creighton H., 1731 Pine St.

1952. Twining, H. Earle, 2026 Delancey St.
1929. Tyson, Ralph M., 255 S. 17th St.
1937. Uhle, Charles A. W., 255 S. 17th St.
1953. Ulin, Alexander W., 230 N. Broad St. (7)
1950. Ullery, John C., 807 Spruce St. (7)
1907. Ullom, Josephus T., Carpenter and Quincy Sts.
1950. Valdes-Dapena, Antonio, 40 Lokesley Rd., Merion, Pa.
1937. Vander Veer, Joseph B., 330 S. 9th St.
1937. Van Loon, Emily Lois, 1930 Chestnut St.
1933. Vastine, Jacob H., 2nd, 136 S. 16th St.
1947. Vastine, Mary F., Woman's Medical College of Pa.
1952. Vischer, Thomas J., 5903 Greene St.
1940. Voegelin, Adrian W., Germantown Professional Bldg.
1941. Vogel, Stoughton R., 246 W. Walnut Lane.
1903. Wadsworth, William S., 4632 Hazel Ave.
1927. Wagers, Arthur J., 1429 Spruce St.
1949. Wagner, Frederick B., Jr., 251 S. 41st St.
1949. Wagner, Joseph A., 2720 Darby Rd., Havertown, Pa.
1928. Wagoner, George W., Medical Bldg., Bryn Mawr, Pa.
1938. Waldman, Joseph, 404 Meadowbrook Lane.
1952. Walker, James M., 3400 Spruce St.
1906. Walker, John K., 139 Little Lane, Haverford, Pa.
1907. Walker, Warren, 511 Lynmere Rd., Bryn Mawr, Pa.
1932. Walkling, Adolph A., 136 S. 16th St.
1932. Watt, Charles C., Jr., 100 W. Coulter St.
1952. Weaver, Harry S., Jr., 37 S. 20th St.
1941. Weaver, Ruth H., 2601 Parkway.
1953. Weber, Lennard L., 255 S. 17th St. (3)
1930. Weeder, S. Dana, 250 W. Tulpehocken St.
1920. Weidman, Fred D., 20 Tenby Rd., Havertown, Pa.
1952. Weinstein, George L., 255 S. 17th St.
1933. Weiss, Benjamin P., The Lenox, 13th and Spruce Sts.
1923. Weiss, Edward, 269 S. 19th St.
1950. Weiss, Sidney, 1930 Chestnut St.
1951. Welty, Jack W., Montgomery Ave. & Owen Rd., Wynnewood, Pa.
1935. Whelan, G. L., 2100 Walnut St.
1921. Whitaker, William, 4645 Oakland St.
1936. White, Ellen Pawling Corson-, Route #2, Fort Myers, Fla.
1925. Widmann, Bernard P., 250 S. 18th St.
1936. Wilder, Theodore S., 6013 Greene St.
1935. Willard, John Harrington, 344 S. 15th St.
1939. Willauer, George, 6129 Greene St.
1907. Williams, Carl, School Lane and Greene St.
1937. Williams, John C., 6370 Germantown Ave.
1920. Williams, Philip F., 355 Bala Ave., Bala-Cynwyd, Pa.
1950. Williams, R. G., Medical School, Univ. of Pa.
1927. Williamson, Ernest G., 6353 Woodbine Ave.
1949. Willson, J. Robert, 3401 N. Broad St.
1921. Wilson, George, 133 S. 36th St.
1945. Wilson, John F., 1930 Chestnut St.
1953. Wilson, Julius L., Henry Phipps Institute, 7th & Lombard Sts. (47)
1942. Wilson, Lucius R., 1305 Morris Road, Wynnewood, Pa.

1937. Wilson, Ross B., 1832 Spruce St. (3)
1949. Wilson, William W., 133 S. 36th St.
1948. Winkelman, Nathaniel W., 1911 Spruce St.
1948. Winston, Julius, 5839 Chester Ave.
1941. Wirts, C. Wilmer, 2017 Delancey St.
1904. Wister, James W., 5430 Germantown Ave.
1953. Wohl, George T., 1727 Pine St. (3)
1933. Wohl, Michael G., 1727 Pine St.
1944. Wolf, Lewis R., 3474 Frankford Ave.
1918. Wolferth, Charles C., 133 S. 36th St.
1942. Wolman, Irving J., 7607 Woodlawn Ave. (26)
1893. Wood, Alfred C., 2035 Walnut St.
1950. Wood, Dorothy D., 2035 Walnut St.
1932. Wood, Francis C., 212 Laurel Lane, Haverford, Pa.
1900. Wood, George B., 329 Hathaway La., Wynnewood, Pa.
1903. Wood, Horatio C., Jr., 319 S. 41st St.
1944. Wood, H. Curtis, Jr., Skippack Pk., Whitemarsh, Pa.
1953. Woodruff, Marston T., 4940 Penn St. (24)
1928. Wright, Carroll S., 1402 Spruce St.
1937. Yaskin, Joseph C., 1832 Spruce St.
1943. Yawger, Nathaniel S., Exeter Rd., Haverford, Pa.
1921. Ylvisaker, Lauritz S., P.O. Box 268, Bryn Mawr, Pa.
1941. Young, Barton R., Germantown Hospital.
1953. Zarafonetis, Chris, 3401 N. Broad St. (40)
1946. Zeigerman, Joseph H., 1836 Delancey St.
1894. Zentmayer, William, 265 Forrest Rd., Merion, Pa.
1952. Zillessen, Frederick O., Jeanes Hospital.
1947. Zintel, Harold A., Univ. of Pa. Hospital.
1949. Zintl, William J., Upper Darby, Pa.
1933. Zulick, J. Donald, Abington Memorial Hospital, Abington, Pa.

Associate Fellows

ELECTED

1951. Shorey, Jeannette McC., 185 Meredith Rd., Rosemont, Pa.
1952. Talbot, Timothy R., Jr., University Hospital, 36th & Spruce Sts.

Non-Resident Fellows

ELECTED

1912. Addison, William H. F., 286 East Sidney Avenue, Mt. Vernon, N. Y.
1941. Aronson, Roland S., Medical Laboratory, Ft. McPherson, Ga.
1934. Bank, Joseph, 800 N. First Ave., Phoenix, Arizona.
1932. Behney, Charles A., 4030-C Urban St., Los Alamos, N. M.
1949. Bixby, Edward W., 61 W. Ross St., Wilkes-Barre, Pa.
1937. Braceland, Francis J., The Institute of Living, 200 Retreat Av., Hartford, Conn.
1948. *Brown, Robert B., U. S. Naval Hospital, Bethesda, Md.

* Military Service.

1952. *Burros, Lt. Harry M., U. S. Naval Hospital, Newport, R. I.
1908. Cadbury, William W., 274 W. Main St., Moorestown, N. J.
1936. Camero, Anthony R., 657 S. Westlake Ave., Los Angeles, Cal.
1941. Cheleden, John, 133 Broadway, Daytona Beach, Fla.
1930. Clarke, Francis Mann, 116 New St., New Brunswick, N. J.
1930. Cottrell, James E., Kennedy Veteran's Administration Hospital, Memphis, Tennessee.
1940. Crowe, Aldrich C., 735 Atlantic Ave., Ocean City, N. J.
1947. Cutler, Norman L., 1300 Harrison St., Wilmington, Del.
1941. *Cuttle, Tracy D., U. S. Naval Hospital. F.P.O. San Francisco, Cal.
1941. Dixon, Harold M., 1624 N. Harrison St., Little Rock, Ark.
1897. Dorland, W. A. Newman, 108 Cedar Ave., Tampa, Fla.
1951. Ellis, Mackinnon, Mountain Home Veteran's Hospital, Mountain Home, Tenn.
1951. Ervin, Carl E., 240 North Third Street, Harrisburg, Pa.
1944. Estes, W. L., Jr., Bethlehem, Pa.
1952. Faller, Constantine P., 127 State St., Harrisburg, Pa.
1940. Forrester, James S., Harrisburg Polyclinic Hospital, Harrisburg, Pa.
1946. Forster, Francis M., Georgetown University Hospital, Washington, D. C.
1947. Gaskill, Herbert S., 250 Ash St., Denver, Colorado.
1913. Gates, Nathaniel, 10 Peterboro, Detroit, Mich.
1931. Gilman, Robert Louis, Cheyney, Pa.
1947. Grady, Hugh G., Armed Forces Institute, Washington, D. C.
1952. Grieco, Reynold M., 2 W. 4th St., Williamsport, Pa.
1936. Guthrie, Donald, 118 S. Wilbur Ave., Sayre, Pa.
1902. Gwyn, Norman B., 109 Madison Ave., Toronto, Canada.
1936. Hatch, Lerleen Clement, 2184 Ayers Ave., Akron, Ohio.
1928. Hayman, Joseph Marchant, Jr., Tufts College Medical School, Boston, Mass.
1933. Hitzrot, Lewis H., Medical Director, Mercersburg Academy, Mercersburg, Pa.
1936. Hughes, Brady A., 312 Euclid Ave., Mt. Brook, Birmingham, Ala.
1953. Imber, Irving, 420 Walnut St., Reading, Pa.
1899. Jopson, John H., Rutherfordton, N. C.
1947. Kelchner, Clyde H., 1125 Turner St., Allentown, Pa.
1931. Kinney, Willard H., 7300 Atlantic Ave., Ventnor, N. J.
1942. Kneedler, William H., 609 N. Statesville Rd., Davidson, N. C.
1944. LaMotte, William O., Medical Arts Building, Wilmington, Del.
1952. Levan, John B., 401 Oley St., Reading, Pa.
1948. Livingood, Clarence S., School of Medicine, Univ. of Texas, Galveston, Texas.
1948. McCall, Milton L., Louisiana State Univ., New Orleans, La.
1948. McLaughlin, John T., 1252 S. Central Ave., Glendale, Calif.
1949. Manlove, Francis R., 535 N. Dearborn St., Chicago, Ill.
1953. Margolies, Michael, 567 E. Chestnut St., Coatesville, Pa.
1935. Mason, James B., 4677 S. 34 St., Arlington, Va.
1935. Matthews, Robert A., 1542 Tulane Ave., New Orleans, La.
1951. *Mayock, Robert L., Fitzsimons A. Hospital, Denver, Colo.
1932. Meade, Richard H., Jr., 750 San Jose Dr., Grand Rapids, Mich.
1936. Middleton, William Shainline, 2114 Adams St., Madison, Wisconsin.
1928. Moon, Virgil H., Univ. of Miami, Coral Gables, Fla.
1949. Motley, Hurley L., Hospital of Good Samaritan, Los Angeles, Calif.
1937. Nicholson, Samuel T., 2d., 642 High St., Pottstown, Pa.
1905. Norris, George W., Dimock, Pa.
1952. Nutt, John B., 416 Pine St., Williamsport, Pa.
1926. Paul, John Rodman, Dept. Internal Medicine, Yale University, New Haven, Conn.
1947. Pearce, Louise, Trevenna Farms, Belle Mead, N. J.

1922. Pleasants, Henry, West Chester, Pa.
1953. Raffensperger, Edward C., 2039 N. 2nd St., Harrisburg, Pa.
1938. Read, Hilton S., 5407 Atlantic Ave., Atlantic City, N. J.
1936. Reisinger, John A., 901 20th St., N. W., Washington, D. C.
1907. Royer, B. Franklin, 429 E. Baltimore St., Greencastle, Pa.
1945. Schell, James F., Veterans Hospital, Wilmington, Del.
1928. Schofield, Frederick S., Veteran's Admin. Hospital, Beckley, W. Va.
1913. de Schweinitz, George L., 85 E. Broad St., Bethlehem, Pa.
1941. Shands, Alfred R., Jr., Alfred I. duPont Institute, Rockland Rd., Wilmington, Del.
1908. Shannon, Charles E. G., 9 Park St., Waterville, Maine
1943. Shewbrooks, Daniel N., The Acacia Mutual Life Ins. Co., Washington, D. C.
1950. Shiffer, Paul H., 111 N. 7th St., Stroudsburg, Pa.
1951. *Shorey, Winston K., 185 Meredith Rd., Rosemont, Pa.
1932. Siegel, Alvin Erdreich, Medical Arts Building, Macon, Ga.
1933. Smelzer, Donald C., Lancaster General Hospital, Lancaster, Pa.
1929. Sponsler, Marshall B., 103 Lansdowne Road, DeWitt, N. Y.
1934. Stewart, Sloan G., Pacific and North Carolina Avenues, Atlantic City, N. J.
1931. Stiles, Merritt H., 820 S. McClellan St., Spokane, Wash.
1952. Sweeney, Francis X., 1420 St. Antoine St., Detroit, Michigan.
1942. Thompson, Wesley D., 18 N. Main St., Lewistown, Pa.
1941. Tompkins, Pendleton, 450 Sutter St., San Francisco, California.
1913. Vail, William Penn, Blairstown, N. J.
1912. Vaux, Norris W., Glenmore Farms, Glen Moore, Pa.
1931. Walker, Herschel Carey, 320 Park Ave., New York City, N. Y.
1914. Willard, De Forrest P., Sea Island, Ga.
1952. Wood, Horatio C., III, 4309 Prospect Rd., Peoria, Ill.

Honorary Fellows

Limited to Fifty, of Whom Twenty May be Foreigners

American

ELECTED

1949. Alexander, John, Univ. of Michigan Hospital Ann Arbor, Mich.
1917. Miner, Charles Howard, B.S., M.D., Member of Board of Directors, Wilkes-Barre General Hospital; Board of Health, Wilkes-Barre; Board of Directors, White Haven Sanitarium Association and Penna. Tuberculosis Society. 264 S. Franklin St., Wilkes-Barre, Pa.
1936. Richards, Alfred Newton, ph.d., sc.d., m.d. (hon.), l.l.d., Emeritus Professor of Pharmacology, School of Medicine and Associate Trustee, University of Pa.
1942. Russell, Frederick Fuller, m.d., Brig. Gen. Med. Corps, U. S. A. (Ret.). 4938 Brownsboro Road, Louisville, Kentucky. d. 12.29.60
1947. Stone, Robert Spencer, Univ. of California Medical School, San Francisco, Calif.

Foreign

1937. Dale, Sir Henry Hallett, c.b.e., f.r.s., m.a., m.d., f.r.c.p., Director, National Institute for Medical Research, The Wellcome Trust, 28 Portman Sq., London, W. C. England.
1922. McCarrison, Sir Robert, k.t., c.i.e., m.d., d.sc., ll.d., f.r.c.p., Major-General, Indian Medical Service (retired). 18 Linton Rd., Oxford, England.

Necrological List

Resident Fellows	*Date of Election*	*Date of Death*
Francis O. Allen	January 3, 1906	April 13, 1953
Herbert B. Carpenter	June 5, 1905	May 26, 1953
Henry Dintenfass	May 9, 1932	August 25, 1953
William Drayton, Jr.	June 11, 1910	March 17, 1953
Henry C. Earnshaw	November 1, 1911	May 22, 1953
Robert S. Gamon	January 8, 1952	May 19, 1953
Alfred Gordon	January 4, 1905	January 12, 1953
Edwin E. Graham	January 3, 1894	June 10, 1953
Harold R. Keeler	May 9, 1938	August 19, 1953
Louis B. Laplace	May 7, 1934	December 27, 1953
Eugene C. Murphy	May 7, 1934	July 9, 1953
Charles A. Steiner	April 2, 1947	September 4, 1953
Herbert W. Taylor	May 8, 1933	August 17, 1953
Louis K. Twyeffort	October 3, 1945	July 30, 1953
Charles C. Watt, Jr.	May 9, 1932	March 18, 1953
Non-Resident Fellows		
Willard H. Kinney	May 11, 1931	August 21, 1952
B. B. Vincent Lyon	May 6, 1914	May 20, 1953
Robert P. McReynolds	December 5, 1900	December 19, 1952
Honorary Fellow		
Warfield T. Longcope	January 8, 1947	April 25, 1953
Honorary Associate Fellow		
William Henry Donner	October 14, 1942	November 3, 1953

Index to Volume 21

Acholia, 162
Acids, sulfur-amino, allergy to in food, 162
Adaptation concept, related to connective tissue diseases (Bauer), 39
Addison's disease and hypertension, 80
Adelizzi, I. R., 81
Adler, F. H., 81, 163
Aegerter, E. E., 90
Aggression, cerebral mechanisms involved, 168
Allen, G. S., 171*
Alvarenga prize lecture (Moore), 106
Anders lecture (Spink), 51
Aneurysms, traumatic arteriovenous, with bilateral 6th nerve palsy, 162
Anger, cerebral mechanisms involved, 168
Appel, K. E., 170*bis
Apresoline, untoward reactions, 162
Armijo, Rolando, 82
Arteries, peripheral, cool box to measure blood flow in diseases of, 162
Astigmia, corneal and total, 163
Atkins, J. P., 81
Austin, J. H. (memoir of), 25
Austin fund, 28

Bach, T. F., 169*
Ballistocardiographic changes following cardiac surgery, 162
Bard, Philip, 168
Batson, O. V., 163
Bauer, Walter, 39
Beardwood, J. T., jr, 80, 162
Bedrossian, R. H., 81
Bell, W. J., jr, 14
Berkowitz, Donald, 162
Beta-radiation therapy, 81
Biliary tract disease, diagnosis using sodium dehydrocholate, 80
Bixby, E. W., jr, 162
Blady, J. V., 170*
Bockus, H. L., 170*
Bone, frontal, eosinophilic granuloma of, 163
Boucot, K. R., 80, 171*
Brazil, communicable disease problems, 82
Breckenridge, R. L., 80
Brody, Henry, 90
Bronchology, 81
Brooks, Frank, 80
Brown, C. L., 170*
Brucellosis (Spink), 51
Building fund, 31
Burnett, W. E., 169*

Cancer, chemotherapy of (Reimann), 1
Cannon, Edward, 81
Cardiovascular diseases, symposium on, 168
Carey, L. S., 169*
Cataract, galactose, 81; c. in alloxan diabetic rabbits, 81
Chambers, W. L., 82
Chance, Burton, 169*
Chile, public health problems, 82
Cimoch, Paul, 80
Clerf, L. H., 81, 171*
Cohen, R. V., 155, 163, 171*
Collagen diseases, (Bauer) 39, 80
Collections, College (ann. rep.), 151
College of Physicians of Phila.: Admin. staff, 171*; Collections (ann. rep.), 151; Committees, 169*; Fellows, 172; Lectures (1953), 168; Library (ann. rep.), 138; Mütter Museum (ann. rep.), 151; Officers, 169*; President's address (Kern), 133; Sections (ann. reps.) 153, (officers) 171*, (programs, abstracts) 80, 162
Committees, College, 169*
Conklin, E. G. (memoir of), 131
Connective tissue diseases, (Bauer) 39, 80
Contributors to College funds, 31
Cool box, to measure blood flow, 162
Cooper, D. A., 80, 169*, 171*
Coronary disease, new classification, 80
Cowan, Alfred, 163
Craven, John, 81
Custer, R. P., 90, 151, 169*, 170*
Cyclodiathermy, 81

Dannenberg, A. M., 170*
Dannenberg, A. M., jr, 90
Davis, Jefferson, 81
Day, R. L., 81
Deaver, J. M., 170*
DeLong, Perce, 81, 171*
Development fund, 28
Diabetes, in diffuse pancreatic disease, 162
Diabetic coma, ketonemia tests, 80
Dixon, J. P., 163
Doane, J. N., jr, 81
Dohan, F. C., 80
Duct, thyroglossal, fistula of, 163
Duncan, G. G., 80bis, 170*

Ear, allergy of, 163
Eimann, John, 80

* Refers to the list of College officers, committees, sections, administrative staff.

Elfman, L. K., 81
English, O. S., 170*bis
Ersner, M. S., 81
Esophagology, 81
Ettelson, L. N., 162
Examinations, medical, 18th c., 14
Exotropia, intermittent, surgical management of, 163

Fellows, list of, 172
Fibroplasia, retrolental, relationship to oxygen, 81
Fitz-Hugh, Thomas, jr, 170*
Flippen, H. F., 82, 170*
Flynn, T. F., 163
Frumin, A. M., 162
Fry, W. E., 171*

Gambescia, J. M., 80
Gastrointestinal haemorrhage, 80
Gastrointestinal pressure recordings, 80
Geckeler, G. D., 168
Germany, western, health problems, 82
Gibbon, J. H., 169*
Gibbon, J. H., Jr, 169*, 170*
Gibson, G. G., 170*
Glaucoma, open angle, 81; malignant, 163; simulated progression of visual field defects, 81
Glover, R. P., 80, 97
Goldsmith, Ralph, 80
Gordon, B. L., 169*
Grant, F. C., 169*
Grant, W. M., 81
Gregory, J. E., 90
Groff, R. A., 81

Hadden, S. B., 170*bis
Haemorrhage, gastrointestinal, 80; postpartum, endocrine dysfunction following, 80
Hafkenschiel, J. H., 162
Hatfield lecture (Reimann), 1
Hauschka, T. S., 90
Havens, W. P., Jr, 170*
Hawthorne, H. R., 162
Haymond, T. A., 82
Heart failure, congestive, effect of ganglion blocking agents, 80
Henle, Werner, 163
Herbut, P. A., 169*
Hitschler, W. J., 163
Hubbard, J. P., 170*
Huber, J. F., 169*
Hughes, Joseph, 170*
Hughes, W. F., jr, 81
Hunter, R. J., 171*
Hypertension and Addison's disease, 80
Hypotony, acute, 81

India, population pressures and public health, 82
Infantilism, pituitary, 168
Infection, intraocular, experimental, with mumps virus, 163
Ingleby, Helen, 90
Ingraham, N. R., jr, 170*
Isard, H. J., 162
Isotope dilution (Moore), 106
Israel, S. L., 80

Jackson, C. L., 81
Jacobs, M. S., 171*
Janton, O. H., 80, 168, 169*
Jeffers, W. A., 80, 171*
Jefferson, Geoffrey, 168

Kate Hurd Mead lecture, 81
Kauffman, M. L., 155
Kelly, G. F. J., 171*
Kelly, H. T., 171*
Kern, R. A., (pres. add.) 133, 169*
Ketonemia tests, 80
Kimbrough, R. A., jr, 170*
Kincaid, J. F., 80
Kirber, H. P., 163
Kirber, M. W., 163
Kirshner, J. J., 80
Knox, K. R., 80
Korea, public health programs, 82
Kornblueh, I. H., 63, 119
Krewson, W. E., 3d, 163, 171*
Krohn, Edward, 82
Krumbhaar, E. B., 131, 169*

LaBoccetta, A. C., 171*
Lachman, Bernard, 81
LaMotte, W. O., jr, 81
Lane, L. L., 168
Lang, O. E., 171*
Lansbury, John, 80, 162, 171*
Lathrop, F. D., 81
Leaman, W. G., jr, 162, 171*bis
Learner, Norman, 80
Lectures, College (1953), 168
Lectures, medical history, 162
Lee, C. C., 82
Lell, W. A., 81
Leopold, I. H., 81
Library (ann. rep.), 138
Lieber, Marshall, 90
Likoff, William, 162, 168
Lima, Louis, 82
Lindauer, M. A., 162
Liu, C. N., 81
Longcope, W. T. (memoir of), 158
Lorber, S. H., 80
Lucchesi, P. F., 171*
Lukens, F. D. W., 158, 169*
Lung carcinoma, routine x-ray detection, 80
Lurie, M. B., 90

Lymphoma, abdominal, diagnosis by presacral air injection, 162
Lyon, B. B. V. (memoir of), 160

Macfarlane, Catharine, 169*
Machella, T. E., 80*bis*
Magasich, Dolores, 171*
Mandible, necrosis, following peritonsillar abscess, 163
Marden, P. A., 171*
Margolies, Alexander, 80
Marino, D. J., 162
Martin, W. L., 169*
Mason, Daniel, 168
Massey, F. C., 168
McClenahan, W. U., 28
McCouch, E. A., 170*
McDaniel, W. B., 2d, 138, 171*
McDonald, P. R., 81, 163
Methionine, in food, allergy to, 162
Miller, M. M., 162, 163
Miller, M. V., 171*
Miller, M. W., 170**bis*
Miller, T. G., 169*
Mitchell oration (Bard), 168
Mitral commissurotomy, 80
Montefiore hospital home care program, 163
Moore, F. D., 106
Morse, E. H., 138, 171*
Mütter lecture (Glover), 97
Mütter Museum (ann. rep.), 151
Mulberger, R. D., 163
Mullen, C. R., 81
Murphy, Foster, 80
Murrell, T. W., 81
Musser lecture (Bauer), 39
Myerson, Ralph, 162
Myocardial infarction, rehabilitation in, 162

Naide, Meyer, 162
Naidoff, David, 81
Neoplasms, bronchial, 81
Nerve, facial, surgery, 81
Nettleship, Anderson, 81
New York Academy of Medicine, Section on Otolaryngology, 81
Nicholson, J. T., 170**bis*
Nickel poisoning, 80
Nodine, J. H., 162
Nose, cavernous tissue of, 163

Officers, College, 169*
Oliver, Jean, 90
O'Neill, T. J. E., 80
Ophthalmoplegia, chronic, progressive, external, 81

Padis, Nicholas, 171*
Palsy, bilateral 6th nerve, 162
Pancreatic disease, diffuse, incidence of diabetes in, 162
Paschkis, K. E., 80, 170*
Pathological Society of Phila., proceedings, 90
Pendergrass, E. P., 170*
Penicillin derivative, otolaryngologic investigation of, 82
Pennys, Raymond, 162
Pepper, O. H. P., 25, 169*
Perloff, W. H., 80, 162
Phila. County Medical Society, 168
Piersol, G. M., 63, 119
Pillsbury, D. M., 170*
Pincus, I. J., 81
Pituitary infantilism, 168
Pneumonitis, 80
Pomeroy, T. C., 90
Primitive medicine, 81
Putney, F. J., 82, 163

Quereau, J. Van D., 162
Quo, Peter, 162

Radbill, S. X, 153, 171*
Randall, Alexander (memoir of), 78
Rao, M. Shama, 82
Rehfuss, M. E., 160
Reimann, S. P., 1
Rhoads, J. E., 169*
Ritter, Joseph, 81
Robbins, Robert, 80, 162
Robertson, W. E., 169*
Rogers, A. M., 163
Ronis, B. J., 163
Rose, Edward, 80, 162
Rothmund, Hildegarde, 82
Rouse, Paul, 162
Royster, H. P., 170*
Rupp, Joseph, 90

Saÿen, J. J., 80
Schaeffer, J. P., 169*, 170*
Scheffey, L. C., 169*
Scheie, H. G., 81, 170*
Schenck, H. P., 163
Schnabel, T. G., jr, 162
Schneeberg, N. G., 80
Schwartz, H., 162
Schwarz, G. A., 81
de Schweinitz lecture (Woods), 163
Scott, M. E., 81
Sections, College, (ann. reps.) 153, (officers) 169*, (programs, abstracts) 80, 162
Serum, protein bound iodine measurements in, 162
Seybolt, J. F., 90
Shay, Harry, 80, 169*
Sheldon, W. F., 80
Shock, postpartum, endocrine dysfunction following, 80
Shoemaker, William, 80
Shryock, R. H., 162

Shuman, C. R., 80
Shuster, A. R., 163
Shuster, B. H., 155, 163, 171*
Silcox, L. E., 82, 163
Silver, G. A., 163
Sinus, lateral, 81
Sinusitis, sarcoid, 163
Smith, A. T., 163
Sokoloff, M. J., 80
Soloff, L. A., 80, 81
Spaeth, Edmund, 162, 171*
Spas of Pa., 63, 119
Sphenoid, malignancy, 163
Spink, W. W., 51
Stadie, W. C., 170*
Steinmetz, C. G., 3d, 81
Stenosis, aortic and mitral, intracardiac surgery for (Glover), 97
Sterling, J. A., 80, 162
Stokes, Joseph, jr, 170*
Strong, George, 90
Strontium^{90} applicator, 81
Stroud, M. W., 3d, 170*
Stroud, W. D., 162, 170*
Students, medical, 18th c., 14; exodus from Phila., 1859, 81
Sturgis, S. B., 170*
Sunderman, F. W., 80bis, 162
Sunderman, F. W., jr, 162
Surgery, intracardiac (Glover), 97
Sussman, Irvin, 162
Swenson, P. C., 169*

Tait, E. F., 163
Temkin, Owsei, 162
Tetanus, tracheotomy in, 82
Tetany, chronic, thyroid gland transplant for, 80
Thomas, J. E., 169*
Thompson, C. M., 80, 153, 171*
Thrombophlebitis, susceptibility to, 162
Thyroid function, revealed by radioactive iodine technics, 80
Thyrotoxicosis, 162
Tittle, C. R., 162
Tocantins, L. M., 169*, 171*
Tonsils, carcinoma, 163
Torsion (ophthalmologic), 162
Town, A. E., 81
Tuberculosis, ocular, 163
Tucker, Gabriel, 81
Tuft, Louis, 162
Tumen, H. J., 162
Twining, H. E., 169*

Uhle, C. A. W., 78
Ulin, Alex, 80
Uremia, serum electrolytes in, 80
Uveal tract, carcinoma of, 81

Valdes-Dapena, A., 90
Vander Veer, J. B., 80, 169*, 170*

Wade, E. N., 171*
Wagner, J. A., 162
Weiss, G. H., 90
Willson, J. R., 80, 170*
Wirts, C. W., 80, 162
Wise, H. M., 80
Wohl, G. T., 162
Wolferth, C. C., 80
Woman's Medical College of Pa., 81
Wood, F. C., 169*
Wood, H. C., jr, 170*
Woods, A. C., 163
Woodward, George (memoir of), 28

Yantes, H. A., 80
Yaskin, Joseph, 162
Young, B. R., 170*

Zappasodi, Peter, 90
Zentmayer prize, 155
Zintel, H. A., 169*

Vol. 21, No. 1
(4th Series)

June
1953

TRANSACTIONS & STUDIES

of the

College of Physicians of Philadelphia

Contents

A Report on Microscopic Progress in the Chemotherapy of Cancer (*Nathan Lewis Hatfield Lecture XXXVII*) ..... Stanley P. Reimann 1

Medical Students and Their Examiners in Eighteenth Century America Whitfield J. Bell, Jr. 14

Memoirs

James Harold Austin (1883–1952) ..... O. H. Perry Pepper 25

George Woodward (1863–1952) ..... William U. McClenahan 28

List of Contributors to the Building, Development, and Austin Funds, and to the Library of the College 31

PUBLISHED AT BALTIMORE, MARYLAND

LLEGE OF PHYSICIANS
LIBRARY
JUN 23 1953
OF PHILADELPHIA

The College of Physicians of Philadelphia does not assume responsibility for statements or views expressed by contributors to the *Transactions & Studies*. The editor checks bibliographic references, to aid in making them factually reliable, and occasionally supplies headings in the text, to facilitate reference to clearly defined portions of the text; the communications are in other respects printed exactly as they were submitted, subject to author corrections on the galleys.

An index to the annual volume of the *Transactions & Studies* appears in the fourth and final (April) number of the volume.

The scientific and historical communications are indexed in: *Biological Abstracts; Current List of Medical Literature; Quarterly Cumulative Index Medicus.*

The Transactions & Studies of the College of Physicians of Philadelphia is published four times a year—June, August, February, April—at Baltimore, Maryland by the College of Physicians of Philadelphia. Subscription, $2 a volume. Single copies, 75 cents.
Publication Office: Mt. Royal and Guilford Aves., Baltimore 2, Md. *Editorial correspondence* should be addressed to: The Editor, College of Physicians of Philadelphia, 19 South 22d Street, Philadelphia-3, Pa. Entered as second class matter June 21, 1938, at the Post Office at Baltimore, Md., under the act of August 24, 1912.
Printed in U. S. A.

The College of Physicians of Philadelphia

Founded 1787

1953

President

Richard A. Kern

Vice-president

Lewis C. Scheffey

Secretary

Leandro M. Tocantins

Treasurer

Francis C. Grant

Censors

John H. Gibbon

Edward B. Krumbhaar

O. H. Perry Pepper

J. Parsons Schaeffer

Honorary Librarian

William Egbert Robertson

Ex-presidential Councillor

T. Grier Miller

Council

The forenamed; the chairmen of the Standing Committees; and the following

elective councillors

Louis H. Clerf

William L. Martin

W. Emory Burnett

William G. Leaman, Jr.

Francis C. Wood

David A. Cooper

Librarian

W. B. McDaniel, 2d

Administrative Associate Librarian

Elliott H. Morse

Curator of the Mütter Museum and Custodian of the College Collections

Ella N. Wade

Clerk of the College

Olga E. Lang

Superintendent

Elliott H. Morse

Assistant Superintendent

George S. Allen

Honorary Director of the Department of Medical Arts

Samuel B. Sturgis

Honorary Legal Counsel

Eric A. McCouch

Committee on Publication

Ernest E. Aegerter, *chairman*

Lawrence S. Carey

H. Earle Twining

Editor of the Transactions & Studies

W. B. McDaniel, 2d

Preceding Number

Vol. 20, No. 4, April, 1953

Contents

President's Address . . . . . Richard A. Kern 125

Annual Reports

Library, 129; Mütter Museum and College Collections, 144; Publication, 146; Sections, 147

Transactions of the Sections: Programs, and Abstracts from the Section on General Medicine 151

Memoirs

Walter Estell Lee (1879–1951) . . . . . Herbert Reid Hawthorne 159

Charles A. E. Codman (1868–1952) . . . . . F. F. Borzell 160

List of the College Lectures, 1952 162

Officers, Committees, Sections, and Administrative Staff of the College, 1953 163

List of the Fellows 166

Index to Volume 20 186

INDEX NUMBER

Vol. 21, No. 4
(4th Series)

April
1954

TRANSACTIONS & STUDIES

of the

College of Physicians of Philadelphia

Contents

President's Address . . . . . Richard A. Kern 133

Annual Reports

Library 138

Mütter Museum and College Collections 151

Sections 153

Memoirs

Edwin E. Graham (1864–1953) . . . . . Edward L. Bauer 156

Warfield Theobald Longcope (1877–1953) . . . . . Francis D. W. Lukens 158

B. B. Vincent Lyon (1880–1953) . . . . . Martin E. Rehfuss 160

Transactions of the Sections: Programs, and Abstracts from the Section on General Medicine 162

List of College Lectures, 1953 168

Officers, Committees, Sections, and Administrative Staff of the College, 1954 169

List of the Fellows 172

Index to Volume 21 193

PUBLISHED AT BALTIMORE, MARYLAND

The College of Physicians of Philadelphia does not assume responsibility for statements or views expressed by contributors to the *Transactions & Studies*. The editor checks bibliographic references, to aid in making them factually reliable, and occasionally supplies headings in the text, to facilitate reference to clearly defined portions of the text; the communications are in other respects printed exactly as they were submitted, subject to author corrections on the galleys.

An index to the annual volume of the *Transactions & Studies* appears in the fourth and final (April) number of the volume.

The scientific and historical communications are indexed in: *Biological Abstracts, Current List of Medical Literature, Quarterly Cumulative Index Medicus.*

The Transactions & Studies of the College of Physicians of Philadelphia is published four times a year—June, August, February, April—at Baltimore, Maryland by the College of Physicians of Philadelphia.
Subscription, $2 a volume. Single copies, 75 cents.
Publication Office: Mt. Royal and Guilford Aves., Baltimore 2, Md. *Editorial correspondence* should be addressed to: The Editor, College of Physicians of Philadelphia, 19 South 22d Street, Philadelphia-3, Pa.
Entered as second class matter June 21, 1938, at the Post Office at Baltimore, Md., under the act of August 24, 1912.
Printed in U. S. A.

The College of Physicians of Philadelphia

Founded 1787

1954

President

Richard A. Kern

Vice-president

Lewis C. Scheffey

Secretary
Leandro M. Tocantins

Treasurer
Francis C. Grant

Censors

John H. Gibbon
Edward B. Krumbhaar
O. H. Perry Pepper
J. Parsons Schaeffer

Honorary Librarian
William Egbert Robertson

Ex-presidential Councillor
T. Grier Miller

Council

The forenamed; the chairmen of the Standing Committees; and the following

ELECTIVE COUNCILLORS

William L. Martin
Francis C. Wood
W. Emory Burnett
David A. Cooper
John H. Gibbon, Jr.
Burgess L. Gordon

Librarian
Elliott H. Morse

Curator of Library Historical Collections
W. B. McDaniel, 2d

Curator of the Mütter Museum and Custodian of the College Collections
Ella N. Wade

Clerk of the College
Olga E. Lang

Superintendent
George S. Allen

Honorary Director of the Department of Medical Arts
Samuel B. Sturgis

Honorary Legal Counsel
Eric A. McCouch

Committee on Publication
Lawrence S. Carey, *chairman*
Francis D. W. Lukens
H. Earle Twining

Editor of the Transactions & Studies
W. B. McDaniel, 2d

Preceding Number

Vol. 21, No. 3, February, 1954

Contents

The Present Status of Intracardiac Surgery for Mitral and Aortic Stenosis (*Thomas Dent Mütter Lecture LXVI*) . . . . . Robert P. Glover 97

Isotope Dilution: a Theory, a Method, a Pathway to New Horizons (*Alvarenga Prize Lecture XIII*) . . . . . Francis D. Moore 106

The Vanishing Spas of Pennsylvania. An Historical Review. Part II. Igho H. Kornblueh and Geo. Morris Piersol 119

Memoir

Edwin Grant Conklin (1863–1952) . . . . . E. B. Krumbhaar 131

C.P.